Electronic Supplementary Information (ESI)

Enantioselective Synthesis of (-)-Paeonilide

Klaus Harrar and Oliver Reiser*

Institut für Organische Chemie, Universität Regensburg,

Universitätsstrasse 31, 93053 Regensburg, Germany

oliver.reiser@chemie.uni-regensburg.de

Table of Contents

Materials and Methods	S2
Experimental Procedures	S3
NMR Spectra	S9
CIF data for **(-)-1**	S19
CIF data for **3**	S24
CIF data for **12**	S29

Materials and Methods

NMR

NMR-spectra were recorded on a FT-NMR-spectrometer of the type Bruker Avance 300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) and Bruker Avance III 600 Kryo (600 MHz for ^{1}H, 150 MHz for ^{13}C). Chemical shifts in parts per million (ppm) from internal $CHCl_3$ (7.26 ppm (^{1}H) and 77.0 ppm (^{13}C)) as standard on the δ scale. Coupling constants are given in Hertz (Hz). The following notations indicate the multiplicity of the signals:
s = singlet, d = doublet, t = triplet, dd = doublet of doublet, ddd = doublet of doublet of doublet, dt = doublet of triplet, td = triplet of doublet, tt = triplet of triplet, ddt = doublet of doublet of triplet, qd = quartet of doublet and m = multiplet.

MS

High resolution mass was recorded on a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000 or Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS at the Central Analytical Laboratory spectrometer (University of Regensburg).

Melting point

The melting points were measured on a Büchi SMP-20 apparatus in a silicon oil bath. Values thus obtained were not corrected.

IR

ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System.

Optical Rotation

The optical rotation was determined in a Perkin Elmer 241 polarimeter at 589 nm wavelength (sodium-d-line) in a 1.0 dm measuring cell of ca. 2 mL volume.

HPLC:

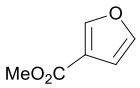
High performance liquid chromatography was carried out using Varian 920-LC with DAD. Phenomenex Lux Cellulose-2 served as chiral stationary phase.

Analytical thin layer chromatography was performed on Merck TLC aluminium sheets silica gel 60 F 254. Visualization was accomplished with UV light (254 nm). For staining vaniline or permanganate solutions followed by heating were used. Liquid chromatography was performed using Merck flash silica gel 60 (0.040-0.063 mm).

Dichloromethane (CH_2Cl_2) was distilled from SICAPENT® and stored over molecular sieves (4 Å). Tetrahydrofurane (THF) was distilled from sodium wire. Ethylacetate (EA) and hexanes (PE) for chromatographic separations were distilled prior to use. Benzoylchloride and pyridine were distilled prior to use.

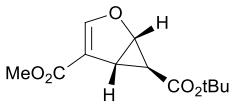
Experimental Procedures

Methyl furan-3-carboxylate (6)



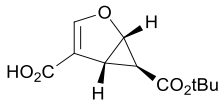
Furan-3-carboxylic acid (**5**) (25.0 g, 223 mmol) was dissolved in 120 mL MeOH. After cooling to 0 °C 25 mL conc. H_2SO_4 were added dropwise. The reaction was stirred for 1 d at room temperature, 50 mL distilled water were added and transferred in a separation funnel. The mixture was extracted with Et_2O (3x100 ml). The combined organic layers were extracted with a saturated $NaHCO_3$ solution, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was distilled at 15 mbar, 85 °C oil bath, 55-60 °C boiling point to yield the ester **6** as colorless oil (23.07 g, 183 mmol, 82%), which solidified while storing at -18 °C. R_f (PE/EE = 3:1) 0.69. IR (neat): $\tilde{\nu}$ 3153, 3000, 2954, 1725, 1579, 1508, 1440, 1310, 1194, 1156, 1075, 984, 874, 793, 760, 601 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.01 - 7.93 (m, 1H), 7.42 - 7.34 (m, 1H), 6.73 - 6.65 (m, 1H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 147.7, 143.8, 119.3, 109.8, 51.5.

(1*S*,5*R*,6*S*)-6-*tert*-butyl 4-methyl 2-oxabicyclo[3.1.0]hex-3-ene-4,6-dicarboxylate (4b)



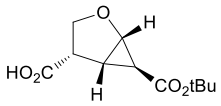
A flame dried flask under nitrogen atmosphere was charged with 3 mL of anhydrous CH_2Cl_2 and $Cu(OTf)_2$ (884 mg, 2.28 mmol, 1.12 mol%). To this suspension (*S*,*S*)-*i*Pr-bis(oxazoline)-ligand **8b** (813 mg, 3.05 mmol, 1.5 mol%) was added, which caused the suspension to turn into a blue solution that was stirred for 1 h. This solution was transferred using a syringe filter to another flame dried flask under nitrogen atmosphere, equipped with a mineral oil bubbler and containing **6** (25.64 g, 203.5 mmol) dissolved in 10 mL CH_2Cl_2 at 0 °C. Phenylhydrazine (225 mL, 2.28 mmol, 1.12 mol%) was added drop wise turning the solution to a dark red-brown color. After 15 min the dropwise addition of *tert*-butyl-diazoglycine (561.5 g solution of 6.7 mass%, 264.6 mmol, 1.3 equiv) in CH_2Cl_2 was started (one drop every 10 sec). During the addition of diazo-compound at 0 °C, nitrogen evolved. After completion, the mixture was allowed to warm to room temperature and was filtered through a plug of basic alumina followed by 500 mL of CH_2Cl_2. The organic layer was concentrated under reduced pressure to afford a yellow-brown oil. The residue was purified by fractioned distillation under reduced pressure (p = 15 mbar, b.p. = 55 - 66 °C) to recover starting material (7.26 g, 77.3 mmol, 38%). The brown residue was purified by column chromatography (PE/EA 15:1) to yield the desired product **4b** as a slightly yellow solid (18.56 g, 77.3 mmol, 38%, brsm: 53%, 83% ee). m.p.: 72 °C. R_f (PE/EA 5:1) 0.61. $[\alpha]_D^{20}$ –20.5 (CH_2Cl_2, c = 1). IR (neat): $\tilde{\nu}$ = 3109, 3071, 2977, 1699, 1599, 1444, 1367, 1271, 1157, 1097, 1045, 975, 830, 792, 760, 720 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.15 (s, 1H), 4.91 (dt, *J* = 5.6, 0.8 Hz, 1H), 3.72 (s, 3H), 2.99 (dd, *J* = 5.6, 2.9 Hz, 1H), 1.41 (s, 9H), 1.01 (dd, *J* = 2.7, 0.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8, 164.2, 156.4, 115.8, 81.5, 68.9, 51.6, 29.1, 28.2, 22.6. HRMS (PI-EIMS, m/z): 240.0999 ($C_{12}H_{16}O_5$, calc. 240.0998 [$M^{+\cdot}$]). HPLC analysis (Phenomenex Lux Cellulose-2, *n*-heptane/*i*PrOH 99:1, 1.0 mL/min, 254 nm): t_r = 13.17, t_r = 17.81; 83% *ee*.

(1*S*,5*R*,6*S*)-6-(*tert*-butoxycarbonyl)-2-oxabicyclo[3.1.0]hex-3-ene-4-carboxylic acid (10)



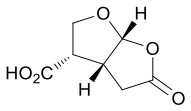
4b (12.31 g, 51.3 mmol) was dissolved in 400 mL of a 3:1 water-THF mixture. To the resulting turbid solution LiOH (1.35 g, 56.4 mmol, 1.1 equiv) was slowly added, which turns the color to yellow. After 6 h of stirring, the reaction mixture was transferred to a separation funnel and washed with Et_2O (2 x 150 mL) to recover remaining starting material (15%). The aqueous layer was acidified with HCl (2 M) to pH 2 and extracted with Et_2O (3 x 150 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the desired product **10** as a colorless solid (9.85 g, 43.6 mmol, 85%, brsm: 100%). m.p.: 142 °C. R_f (PE/EA 1:1) 0.26. $[\alpha]_D^{20}$ –23.8 (MeOH, c = 1). IR (neat): $\tilde{\nu}$ 3038, 2976, 1711, 1655, 1602, 1447, 1385, 1365, 1275, 1159, 1107, 975, 897, 836, 760, 717 cm^{-1}. ^1H NMR (300 MHz, Acetone): δ 10.22 (s, 1H), 7.36 (s, 1H), 5.03 (d, *J* = 5.6 Hz, 1H), 2.92 (dd, *J* = 5.6, 2.8 Hz, 1H), 1.44 (s, 10H), 1.05 (d, *J* = 2.6 Hz, 1H). ^{13}C NMR (75 MHz, Acetone): δ 171.2, 164.8, 157.6, 116.7, 81.6, 69.3, 29.7, 28.2, 22.9. HRMS (EI-MS, m/z): 226.0841 ($C_{11}H_{14}O_5$, calc. 226.0841 [$M^{+\cdot}$]).

(1*S*,4*S*,5*S*,6*S*)-6-(*tert*-butoxycarbonyl)-2-oxabicyclo[3.1.0]hexane-4-carboxylic acid (11)



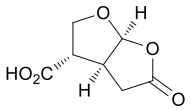
10 (9.30 g, 41.2 mmol) was dissolved in 200 mL of an EtOH/water mixture (95:5) and 900 mg Pd/C (10%) were added. After two times vacuum-hydrogen-flashing, hydrogen was applied via a balloon. When the starting material was consumed (about 4 h), the mixture was filtered through celite and washed with 100 mL EtOH, twice. The organic layer was concentrated under reduces pressure to afford the desired product **11** as colorless oil (9.40 g, 41.2 mmol, 100%) which solidified after some days. m.p.: 92 °C. R_f (PE/EA 1:1) 0.2. $[\alpha]_D^{20}$ +62.4 (MeOH, c = 1). IR (neat): $\tilde{\nu}$ 3192, 2984, 1703, 1401, 1366, 1320, 1197, 1152, 1116, 1073, 981, 952, 870, 841, 779, 725, 674 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 10.94 (s, 1H), 4.22 - 4.11 (m, 2H), 3.68 (t, *J* = 9.8 Hz, 1H), 3.41 (td, *J* = 9.5, 5.4 Hz, 1H), 2.40 (td, *J* = 5.4, 3.8 Hz, 1H), 2.20 (dd, *J* = 3.7, 0.9 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.3, 169.9, 81.3, 67.9, 65.8, 44.4, 28.2, 27.5, 22.9. HRMS (ESI-MS, m/z): 227.0927 ($C_{11}H_{15}O_5$, calc. 227.0925 [$(M-H)^-$]).

(3*S*,3*aR*,6*aR*)-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (12)



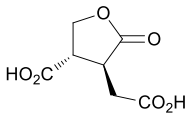
11 (2.64 g, 11.6 mmol) was dissolved in 30 mL THF and cooled to 0 °C. To the cooled solution 90 mL HCl (2 M) were added dropwise within 1 h. The resulting mixture was allowed to warm to room temperature and stirred for 12 h. The solvent was evaporated under reduced pressure to afford the crude product as brownish solid and was used without further purification. For analytical reasons a small sample of the crude product was purified by silica column chromatography (toluene/ethyl formate/formic acid = 5:4:1). m.p. 170 °C. R_f (toluene/ethyl formate/formic acid 5:4:1) = 0.28. $[\alpha]_D^{20}$ –52 (MeOH, c = 1). IR (neat) ṽ 3086, 3008, 2904, 1773, 1711, 1416, 1367, 1295, 1244, 1182, 1132, 1103, 966, 843, 802, 735, 664 cm^{-1}. ^1H NMR (600 MHz, DMSO): δ 12.86 (s, 2H), 6.08 (d, *J* = 5.4 Hz, 2H), 4.12 (dd, *J* = 9.0, 7.6 Hz, 2H), 3.87 (dd, *J* = 10.9, 9.1 Hz, 2H), 3.41 (ddd, *J* = 15.4, 10.3, 5.0 Hz, 2H), 3.30 (ddd, *J* = 10.9, 9.0, 7.6 Hz, 3H), 2.81 (dd, *J* = 18.8, 10.6 Hz, 2H), 2.37 (dd, *J* = 18.8, 4.7 Hz, 2H). ^{13}C NMR (151 MHz, DMSO): δ 175.1, 171.5, 107.8, 67.4, 46.3, 39.8, 29.9. HRMS (EI-MS, m/z): 173.0454 ($C_7H_9O_5$, calc. 173.0450 [MH^+]).

(3*S*,3*aS*,6*aS*)-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (3)



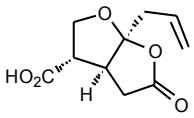
Crude **12** (2.00 g, 11.6 mmol) was dissolved in pyridine (10 mL) together with 10 drops of water and was stirred for 2 h at room temperature. Pyridine was removed by co-distillation with toluene (3 x 5 mL) under reduced pressure. The crude mixture was purified by silica column chromatography (toluene/ethyl formate/formic acid = 5:4:1) to afford the desired product **3** as slightly yellow solid (1.49 g, 8.66 mmol, 75% based on **11**). m.p. 143 °C. R_f (toluene/ethyl formate/formic acid 5/4/1) 0.28. $[\alpha]_D^{20}$ –19.2 (MeOH, c = 1). IR (neat): ṽ 2994, 1771, 1695, 1416, 1358, 1295, 1178, 1103, 966, 929, 885, 855, 803, 670, 614 cm^{-1}. ^1H NMR (300 MHz, MeOD): δ 6.10 (d, *J* = 5.5 Hz, 1H), 4.31 (dd, *J* = 9.5, 2.1 Hz, 1H), 4.12 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.61 - 3.50 (m, 1H), 3.09 - 2.90 (m, 2H), 2.61 (dd, *J* = 18.8, 3.7 Hz, 1H). ^{13}C NMR (75 MHz, MeOD): δ 177.6, 175.3, 110.2, 70.6, 51.2, 43.1, 34.7. HRMS (ESI-MS, m/z): 171.0298 ($C_7H_7O_5$, calc. 171.0299 [$(M-H)^-$]).

(3*S*,4*S*)-4-(carboxymethyl)-5-oxotetrahydrofuran-3-carboxylic acid (13)



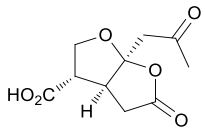
3 (1.41 g, 8.2 mmol) was dissolved in 25 mL acetone and cooled to 0 °C. Within 30 min 8.2 mL Jones-reagent (2.5 M) were added. The mixture turned slowly from orange to green. After 6 h it was transferred to a separation funnel, 10 mL of water were added and it was washed with EA (4 x 25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by silica column chromatography (PE/EA = 1:2 + HOAc (1 vol%)) to afford the desired product **13** as a sticky oil (1.36 g, 7.23 mmol, 88%). R_f (PE/EA = 1:2 + HOAc (1 vol%)) = 0.08. $[\alpha]_D^{20}$ = -29.5 (MeOH, c = 1). IR (neat) $\tilde{\nu}$ =3506.3321, 2977, 1721, 1699, 1408, 1380, 1259, 1188, 1158, 1085, 1029, 861, 714, 692, 648 cm^{-1}. ^1H NMR (600 MHz, CD_3CN): δ = 4.49 (t, *J* = 9.1 Hz, 1H), 4.28 (t, *J* = 9.1 Hz, 1H), 3.42 (dt, *J* = 10.2, 9.1 Hz, 1H), 3.11 (dt, *J* = 10.6, 5.4 Hz, 1H), 2.76 (d, *J* = 5.8 Hz, 2H). ^{13}C NMR (151 MHz, CD_3CN): δ = 177.7, 172.9, 172.7, 68.0, 45.5, 39.8, 33.9. HRMS (ESI-MS, m/z): 187.0247 ($C_7H_7O_6$, calc. 187.0248 [(M-H)$^-$]).

(3*S*,3*aS*,6*aS*)-6*a*-allyl-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (2)



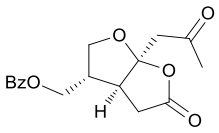
In a flame dried flask under nitrogen atmosphere **13** (603 mg, 3.32 mmol) was dissolved in 50 mL of dry THF and cooled to –78 °C. Allylmagnesium bromide (8.02 mL of a 1M solution in Et_2O, 8.02 mmol, 2.5 equiv) was added dropwise. The turbid solution was kept at this temperature for 2 h, and subsequently brought to 0 °C. After transfer to a separation funnel, 20 mL of water were added. The mixture was acidified to pH 2 by HCl (2 M), and extracted with Et_2O (4 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica column chromatography (toluene/ethyl formate/formic acid = 5:4:1) to afford **2** as colorless oil (514 mg, 2.42 mmol, 73%). R_f (toluene/ethyl formate/formic acid 5:4:1) 0.35. $[\alpha]_D^{20}$ –16 (MeOH, c = 1). IR (neat) $\tilde{\nu}$ 3402, 2930, 2848, 1716, 1648, 1414, 1263, 1208, 1089, 1017, 972, 924, 866 cm^{-1}. ^1H NMR (300 MHz, Acetone): δ 5.81 (ddt, *J* = 17.3, 10.2, 7.1 Hz, 1H), 5.28 - 5.06 (m, 2H), 4.31 (dd, *J* = 9.5, 2.2 Hz, 1H), 4.15 (dd, *J* = 9.5, 6.6 Hz, 1H), 3.38 (dt, *J* = 10.4, 2.7 Hz, 1H), 3.20 - 3.10 (m, 1H), 3.01 (dd, *J* = 18.7, 10.4 Hz, 1H), 2.75 - 2.58 (m, 3H). ^{13}C NMR (75 MHz, Acetone): δ 174.6, 173.7, 132.3, 120.1, 118.6, 70.1, 51.6, 44.6, 41.9, 35.9. HRMS (ESI-MS, m/z): 211.0612 ($C_{10}H_{11}O_5$, calc. 211.0612 [(M-H)$^-$]).

(3*S*,3*aS*,6*aS*)-5-oxo-6*a*-(2-oxopropyl)hexahydrofuro[2,3-*b*]furan-3-carboxylic acid (14)



2 (100 mg, 0.47 mmol) was dissolved in 2 mL of acetone/water (4:1) and cooled to 0°C. At that temperature $Hg(OAc)_2$ (37.4 mg, 0.118 mmol, 0.25 equiv) was added, which turned the solution yellow. After 15 min Jones-reagent (470 µL, 2.5 M) was added dropwise. The mixture was allowed to warm to room temperature and stirred for additional 15 h, transferred to a separation funnel, mixed with 1 mL of water and extracted with Et_2O (4 x 3 ml). The crude product was purified by silica column chromatography (toluene/ethyl formate/formic acid 5:4:1) to afford the desired product **14** as yellow oil (85 mg, 0.37 mmol, 79%). R_f (toluene/ethyl formate/formic acid = 5:4:1) 0.22. $[\alpha]_D^{20}$ –30.7 (MeCN, c = 1). IR (neat) ṽ 3503, 2998, 2919, 1766, 1712, 1404, 1373, 1275, 1205, 1173, 1112, 1036, 999, 949, 926, 862, 653, 609 cm^{-1}. ^1H NMR (600 MHz, CD_3CN): δ 4.22 (d, *J* = 9.7 Hz, 1H), 4.02 (dd, *J* = 9.8, 6.0 Hz, 1H), 3.37 - 3.34 (m, 1H), 3.30 (d, *J* = 23.0 Hz, 1H), 3.15 (dd, *J* = 18.7, 10.9 Hz, 1H), 3.03 (d, *J* = 18.1 Hz, 1H), 2.98 (d, *J* = 6.0 Hz, 1H), 2.54 (dd, *J* = 18.7, 3.6 Hz, 1H), 2.12 (s, 3H). ^{13}C NMR (151 MHz, CD_3CN) δ 206.2, 175.9, 174.0, 116.2, 69.4, 51.8, 49.9, 45.2, 36.3, 30.9. HRMS (ESI-MS, m/z): 227.0563 ($C_{10}H_{11}O_6$, calc. 227.0561 [$(M-H)^-$]).

((3*S*,3*aS*,6*aS*)-5-oxo-6*a*-(2-oxopropyl)hexahydrofuro[2,3-*b*]furan-3-yl)methyl benzoate (-)-(1)

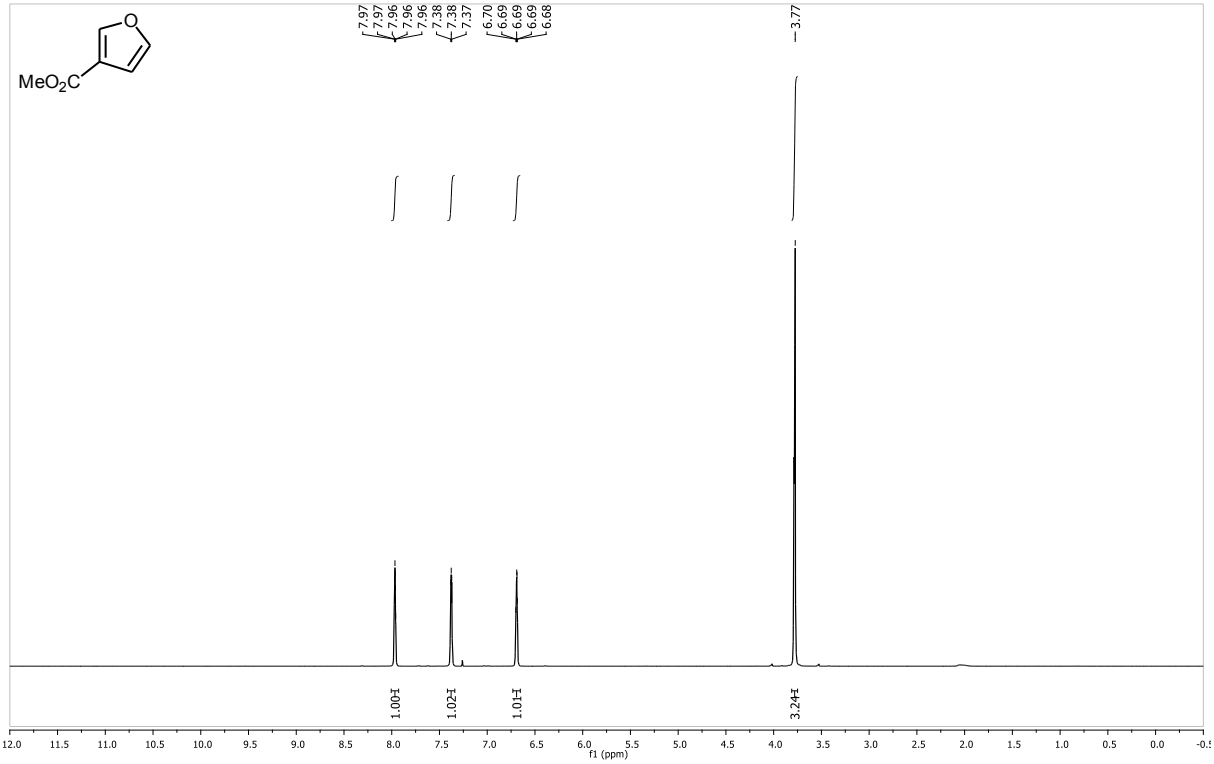


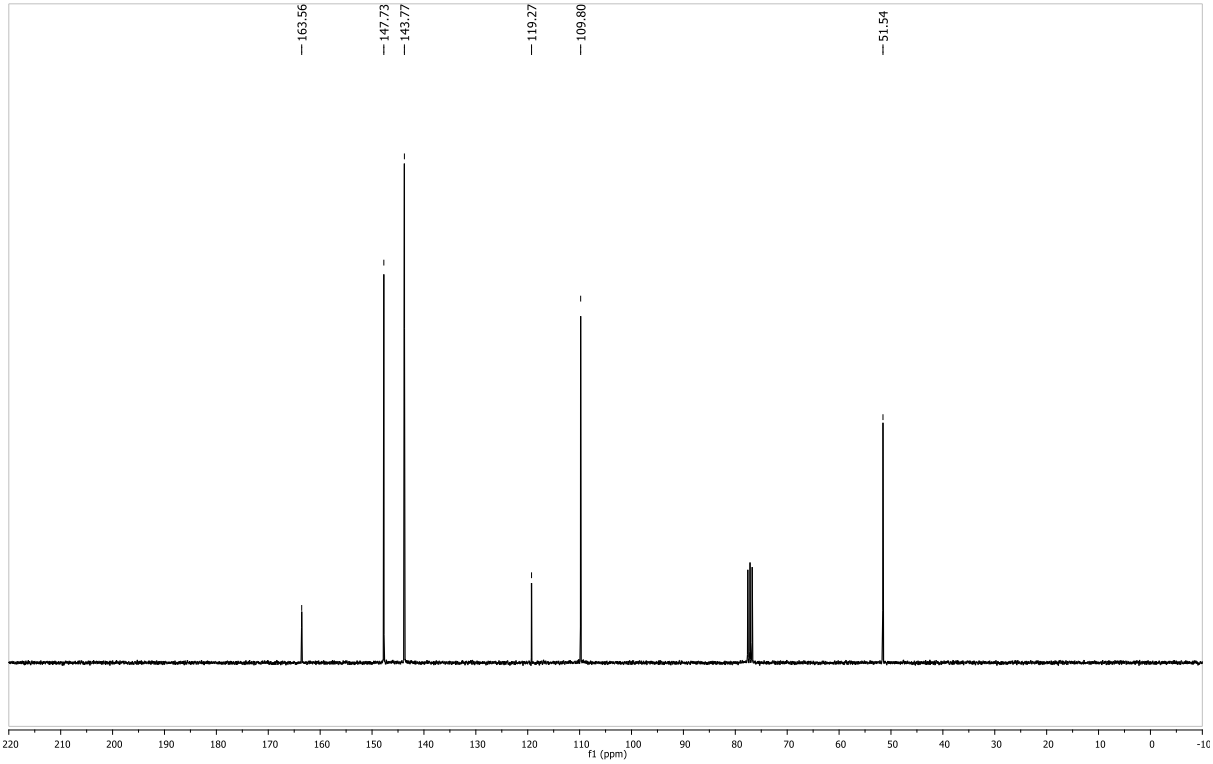
In a flamed dried flask under nitrogen atmosphere **14** (18 mg, 0.079 mmol) was dissolved in 1 mL of dry THF and cooled to –15 °C. To this solution BH_3·THF (1 M in THF, 166 µL, 0.166 mmol, 2.1 equiv) was added dropwise. After 4 h at –15 °C the mixture was allowed to warm to room temperature. The solvent was evaporated under reduced pressure, and the residue was dissolved in 1.5 mL of dry CH_2Cl_2, cooled to –40 °C and treated with DMAP (1 mg, 0.008 mmol, 0.1 equiv), triethylamine (66 µL, 0.474 mmol, 6 equiv) and benzoyl chloride (10 µL, 0.083 mmol, 1.05 equiv). The reaction mixture was allowed to warm to –10 °C. After 1.5 d it was transferred to a separation funnel, treated with 1 mL of a half saturated NH_4Cl solution and extracted with Et_2O (3 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was dissolved in 2 mL of dry CH_2Cl_2, cooled to 0 °C and treated with solid Dess-Martin Periodinane (DMP; 33.5 mg, 0.079 mmol, 1 equiv). After 3 h at that temperature it was warmed to room temperature and transferred to a separation funnel. The mixture was washed with saturated $NaHCO_3$ solution (2 x 1 mL). The combined aqueous layers were extracted with CH_2Cl_2 (2 x 1 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica column chromatography (PE/EA = 2:1) and crystallized from methanol to afford the clean product (-)-**1** as white needles (11 mg, 0.035 mmol, 44% based on **14**). m.p.: 152 °C. R_f (PE/EA) 0.5. $[\alpha]_D^{20}$ –42 ($CHCl_3$, c = 0.14). IR (neat) ṽ = 2959, 2925, 2855, 1762, 1705, 1370, 1274, 1209, 1176, 1111, 1040, 947, 921, 709 cm^{-1}. ^1H

NMR (600 MHz, $CDCl_3$): δ 8.02 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.60 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 4.29 (dd, *J* = 11.0, 7.3 Hz, 1H), 4.19 (dd, *J* = 11.0, 8.0 Hz, 1H), 4.03 (qd, *J* = 9.9, 3.4 Hz, 2H), 3.40 (d, *J* = 17.7 Hz, 1H), 3.34 (dd, *J* = 18.6, 10.5 Hz, 1H), 2.99 - 2.93 (m, 2H), 2.58 - 2.51 (m, 2H), 2.20 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 204.5, 174.6, 166.5, 133.6, 129.8, 129.7, 128.7, 115.1, 68.1, 65.1, 49.7, 46.9, 44.6, 36.8, 31.1. HRMS (ESI-MS, m/z): 319.1180 ($C_{17}H_{19}O_6$, calc. 319.1176 [$(M+H)^+$]).

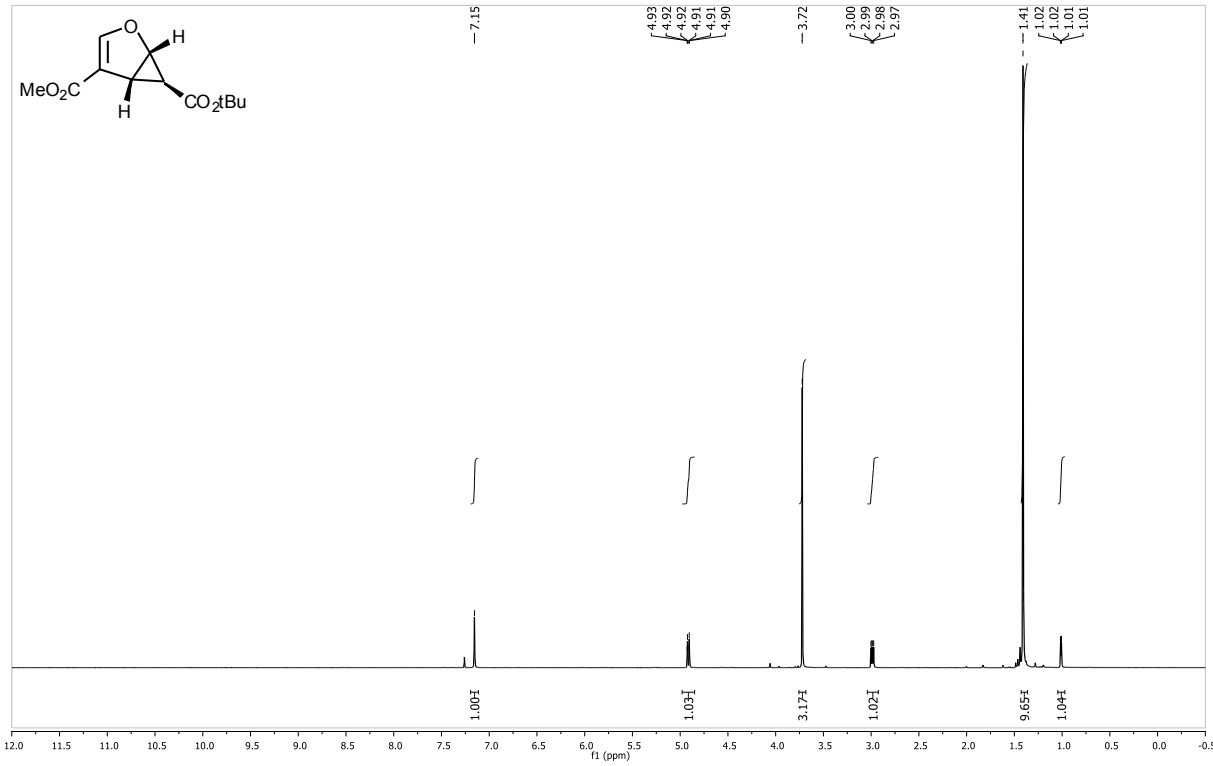
NMR Spectra

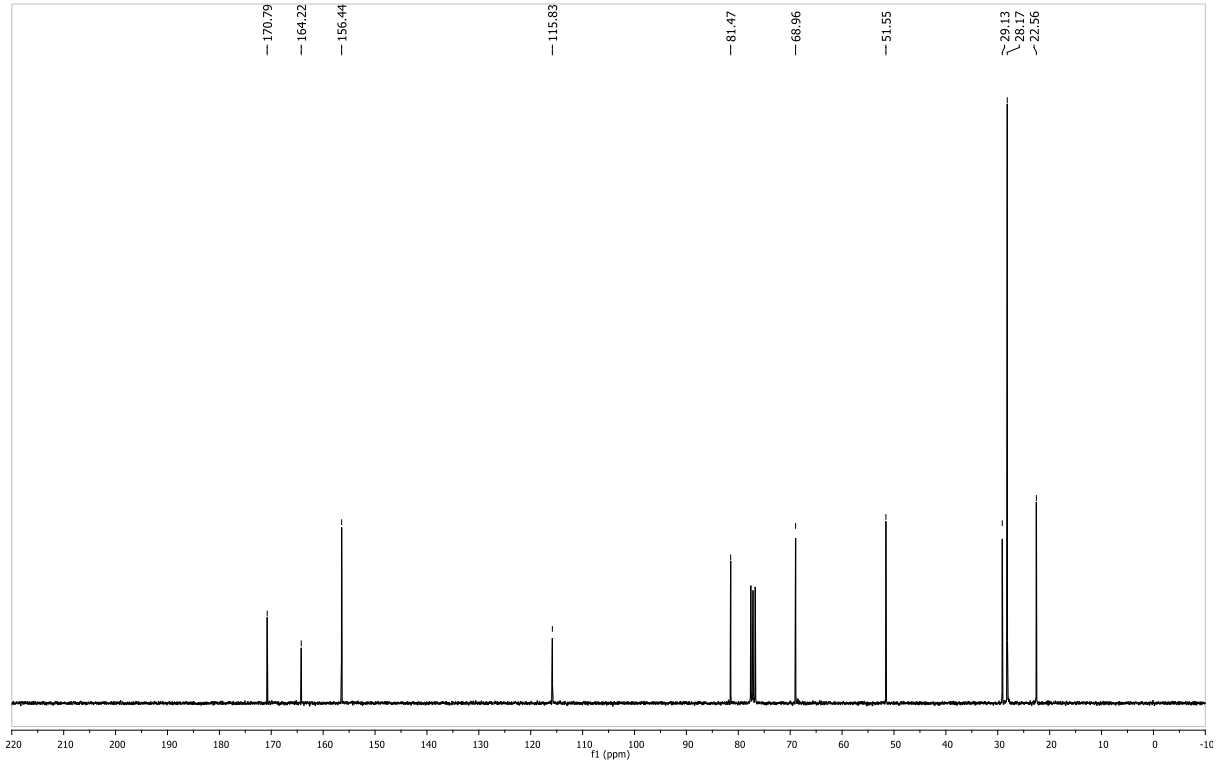
Methyl furan-3-carboxylate (6)



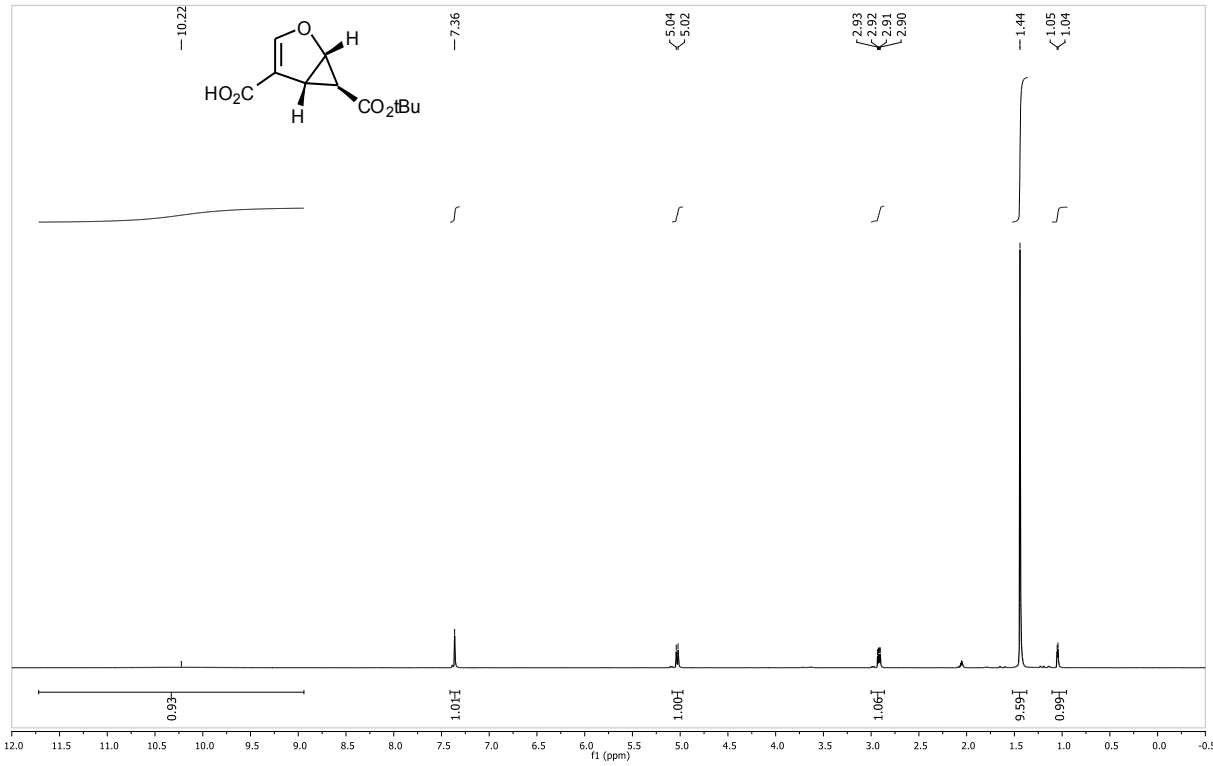


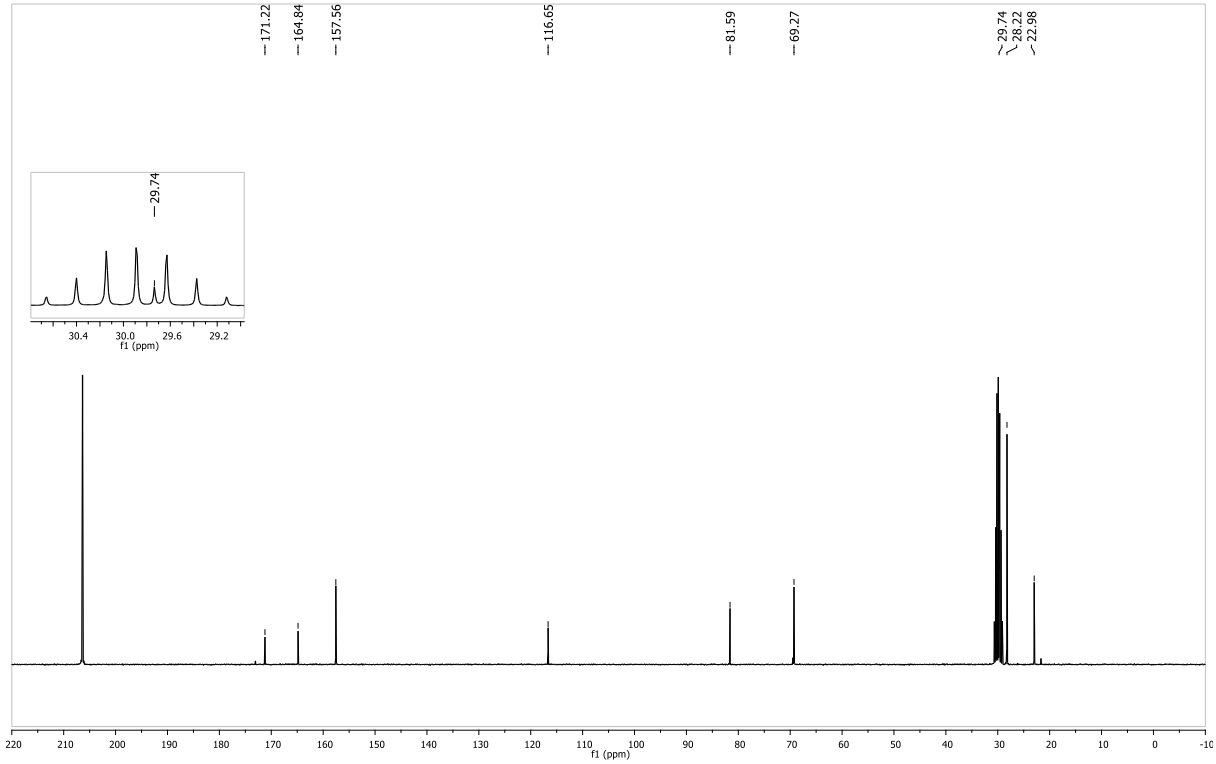
(1*S*,5*R*,6*S*)-6-*tert*-butyl 4-methyl 2-oxabicyclo[3.1.0]hex-3-ene-4,6-dicarboxylate (4b)



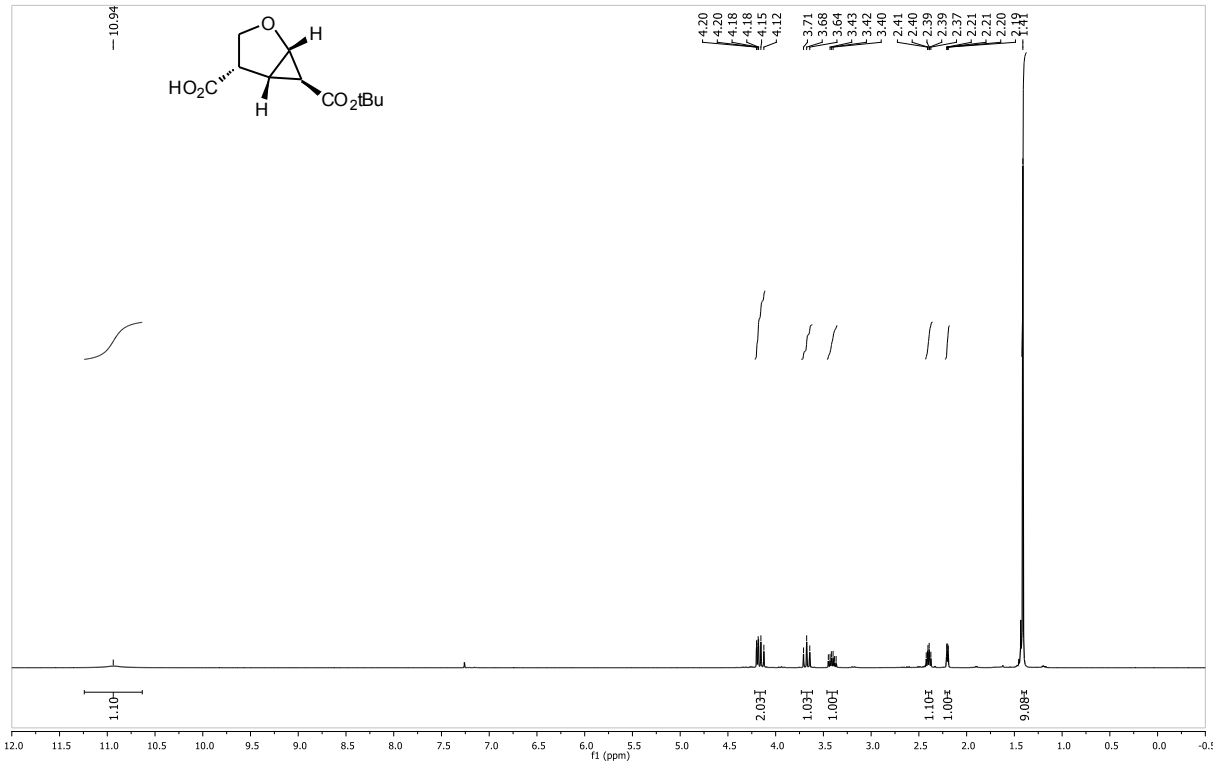


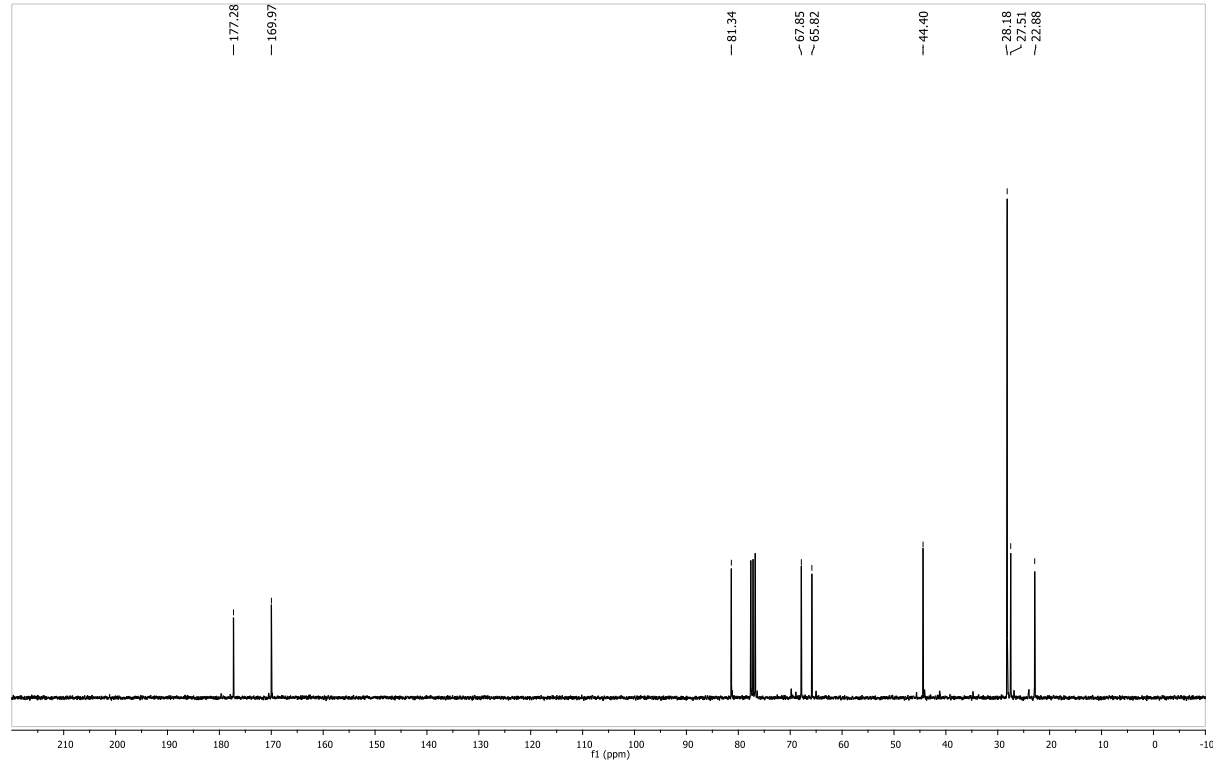
(1*S*,5*R*,6*S*)-6-(*tert*-butoxycarbonyl)-2-oxabicyclo[3.1.0]hex-3-ene-4-carboxylic acid (10)



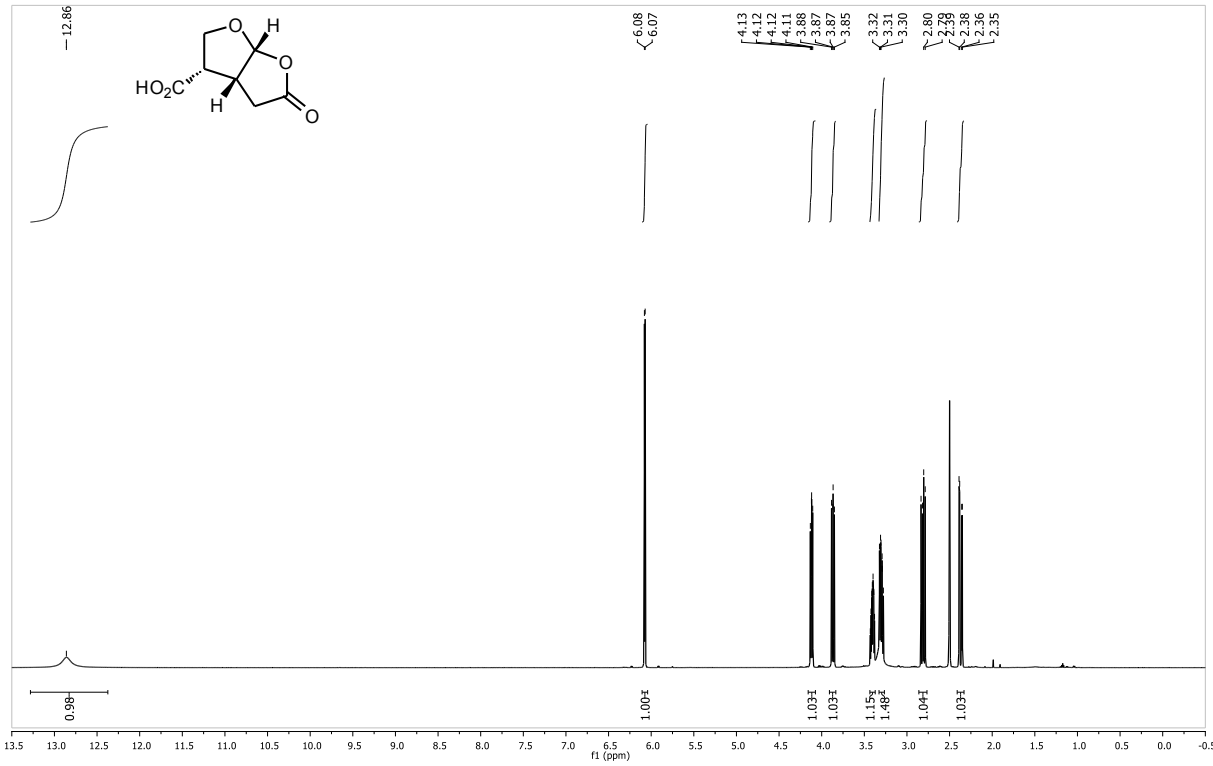


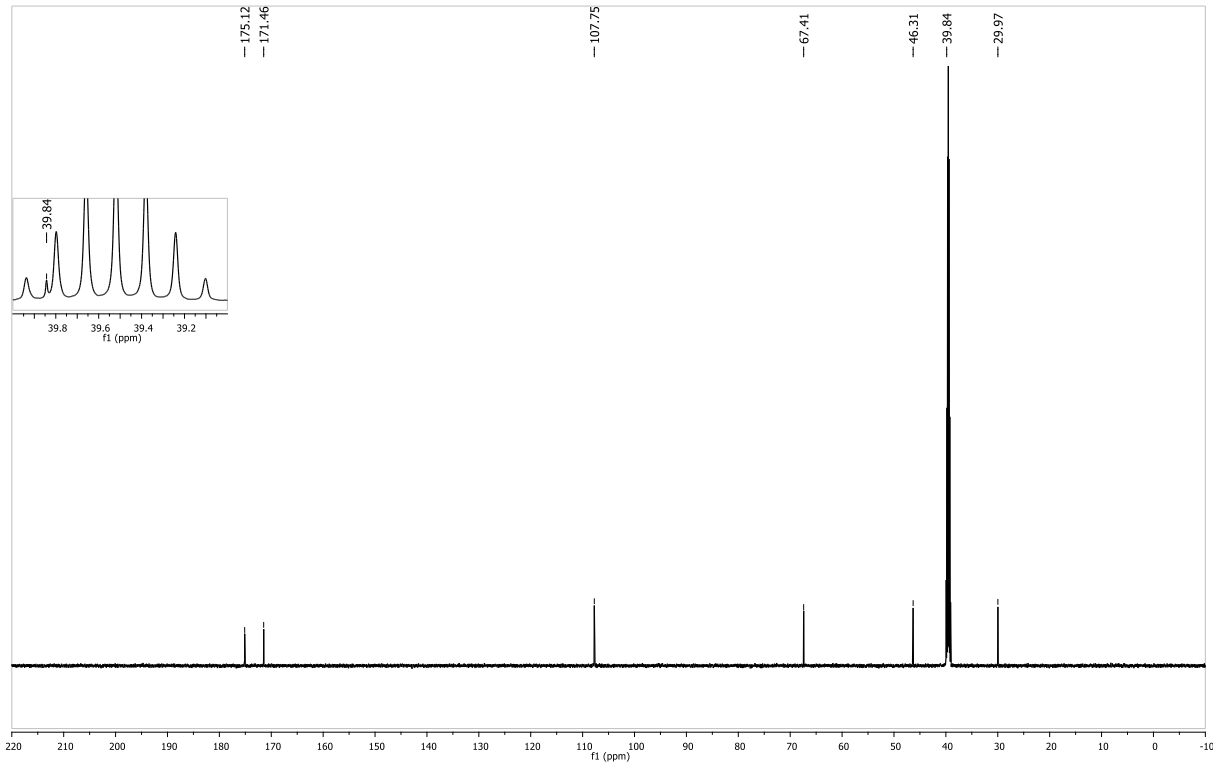
(1*S*,4*S*,5*S*,6*S*)-6-(*tert*-butoxycarbonyl)-2-oxabicyclo[3.1.0]hexane-4-carboxylic acid (11)



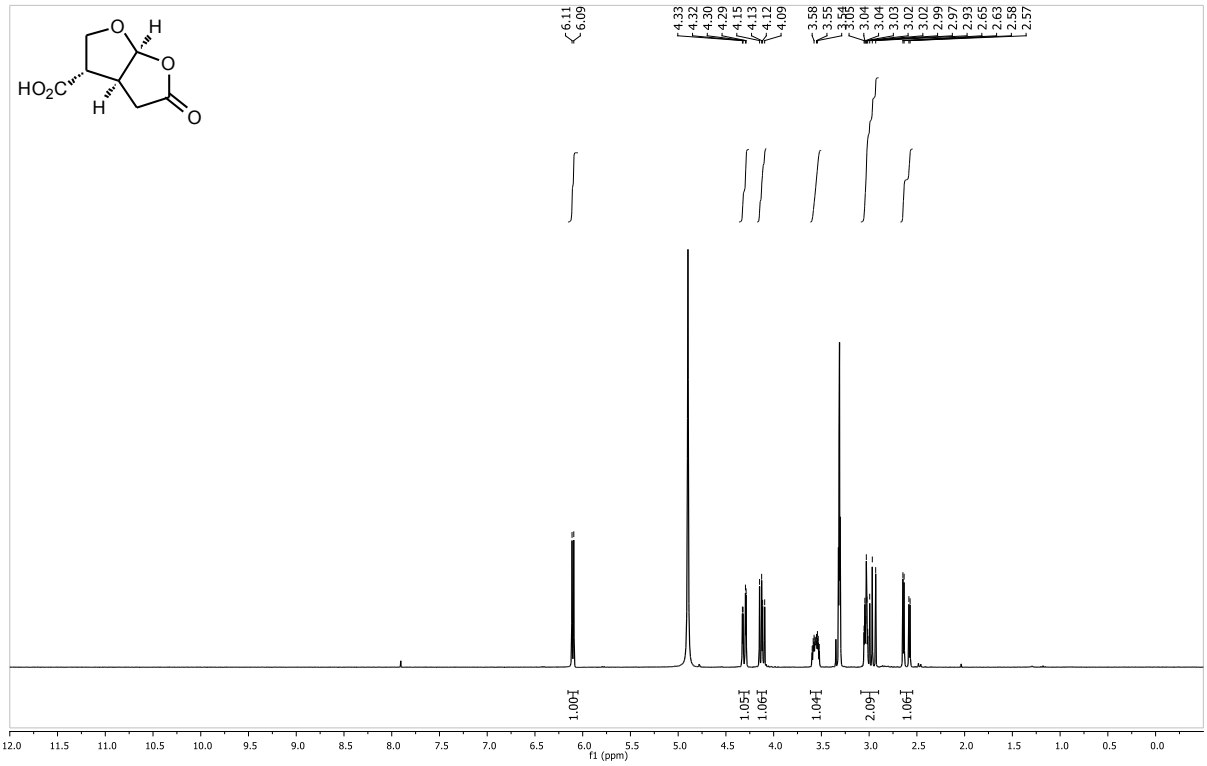


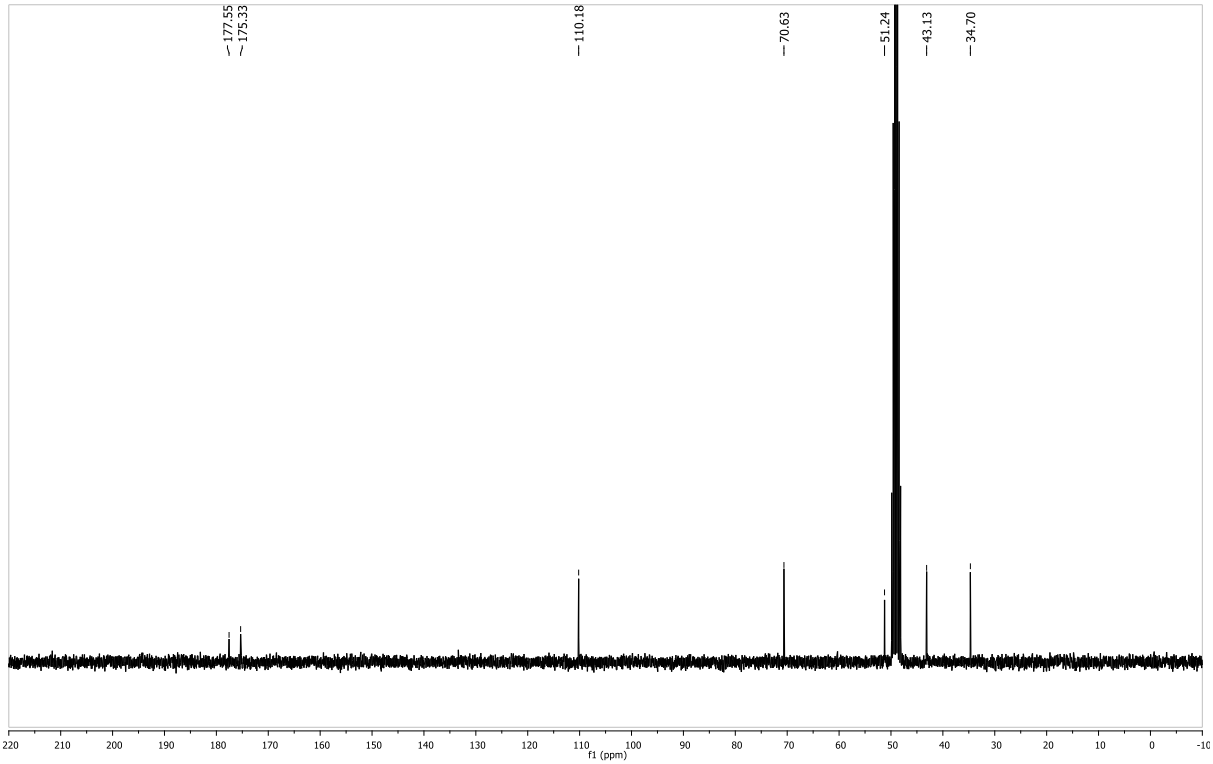
(3*S*,3*aR*,6*aR*)-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (12)



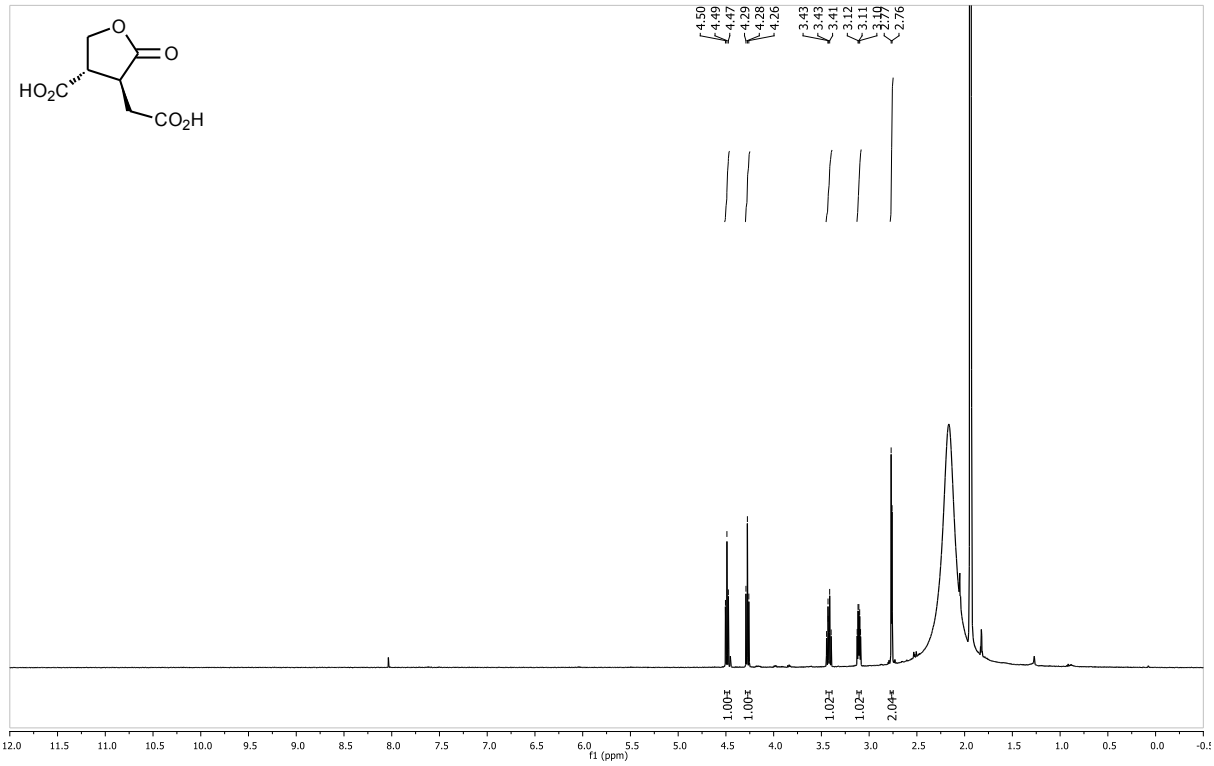


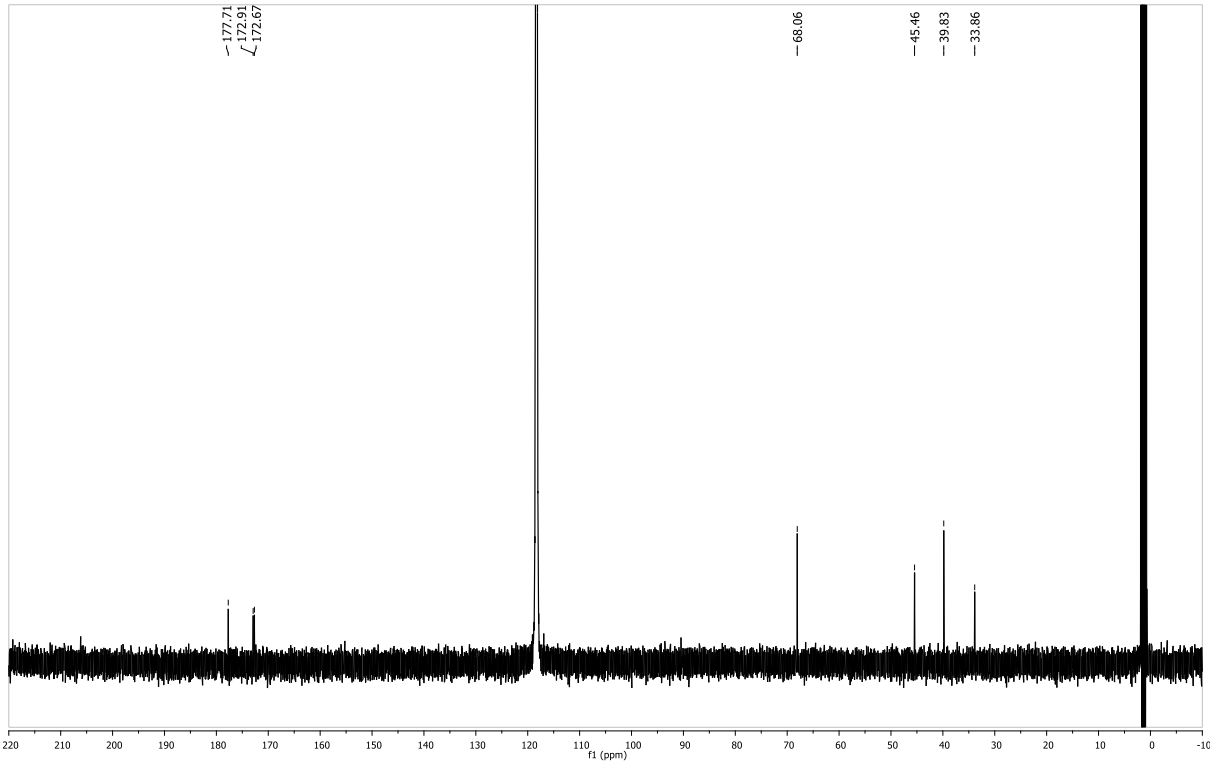
(3*S*,3*aS*,6*aS*)-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (3)



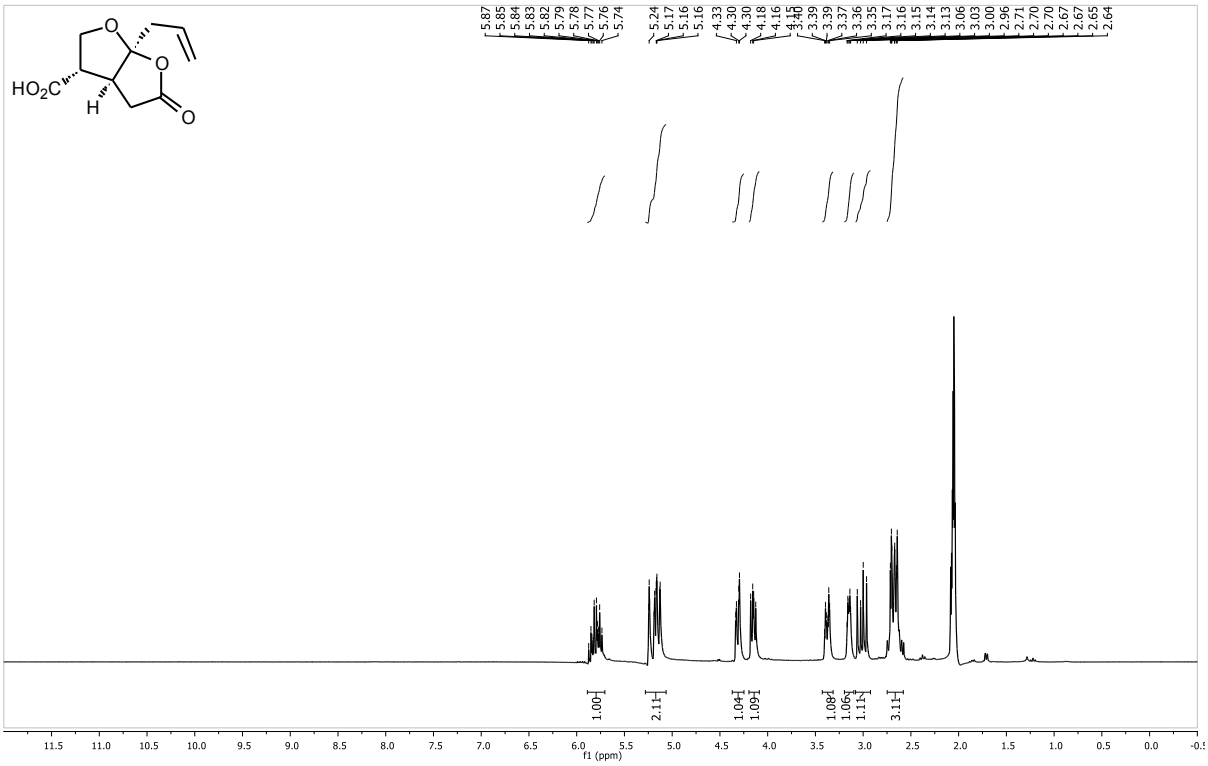


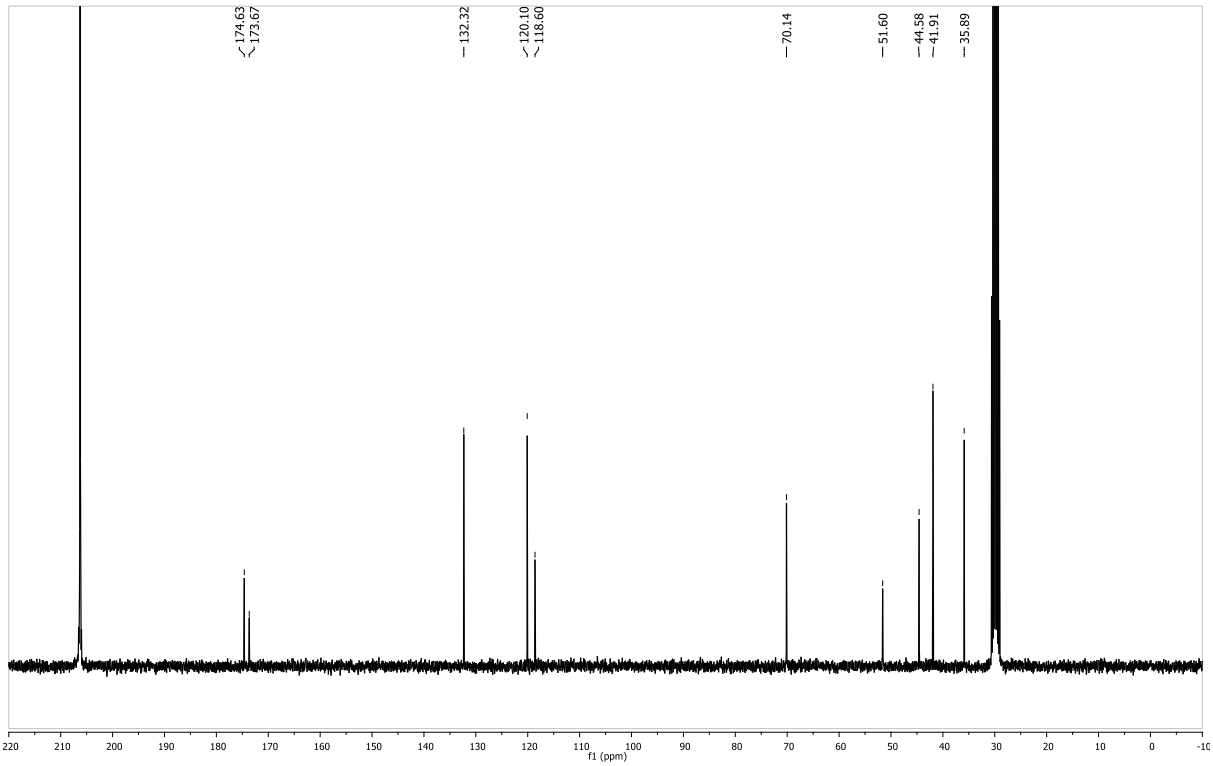
(3*S*,4*S*)-4-(carboxymethyl)-5-oxotetrahydrofuran-3-carboxylic acid (13)



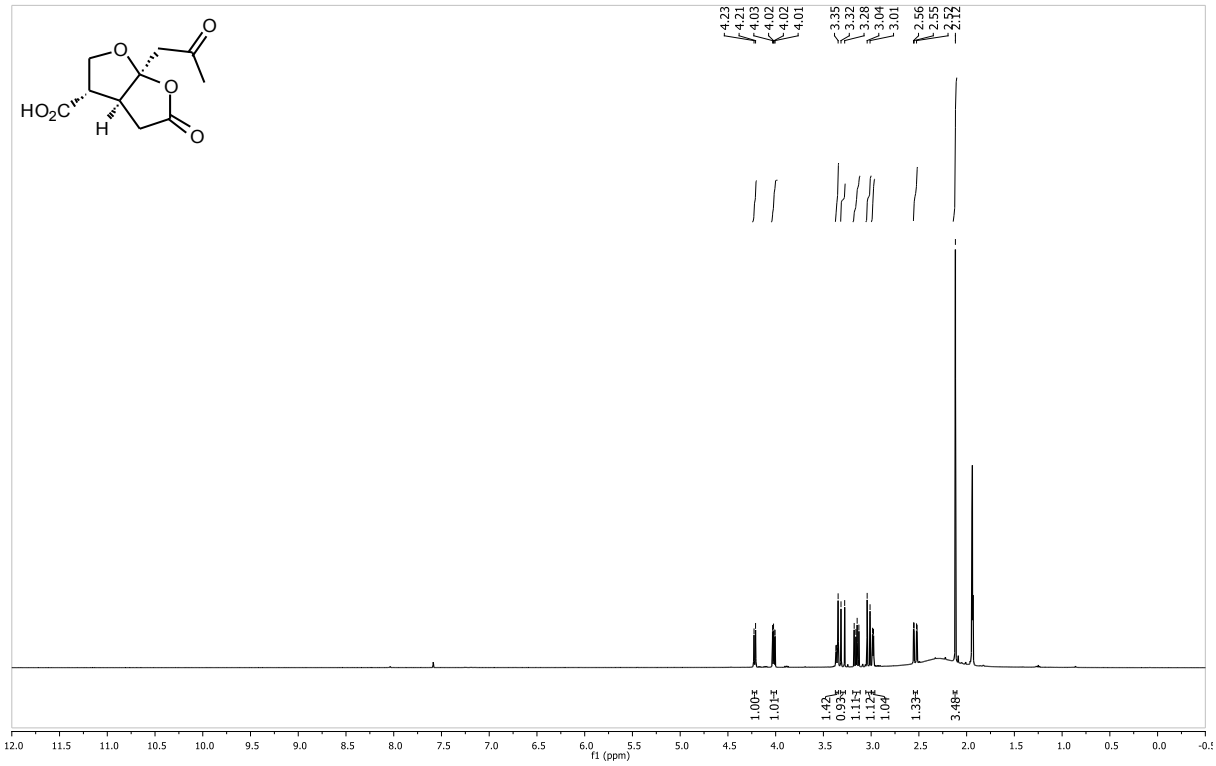


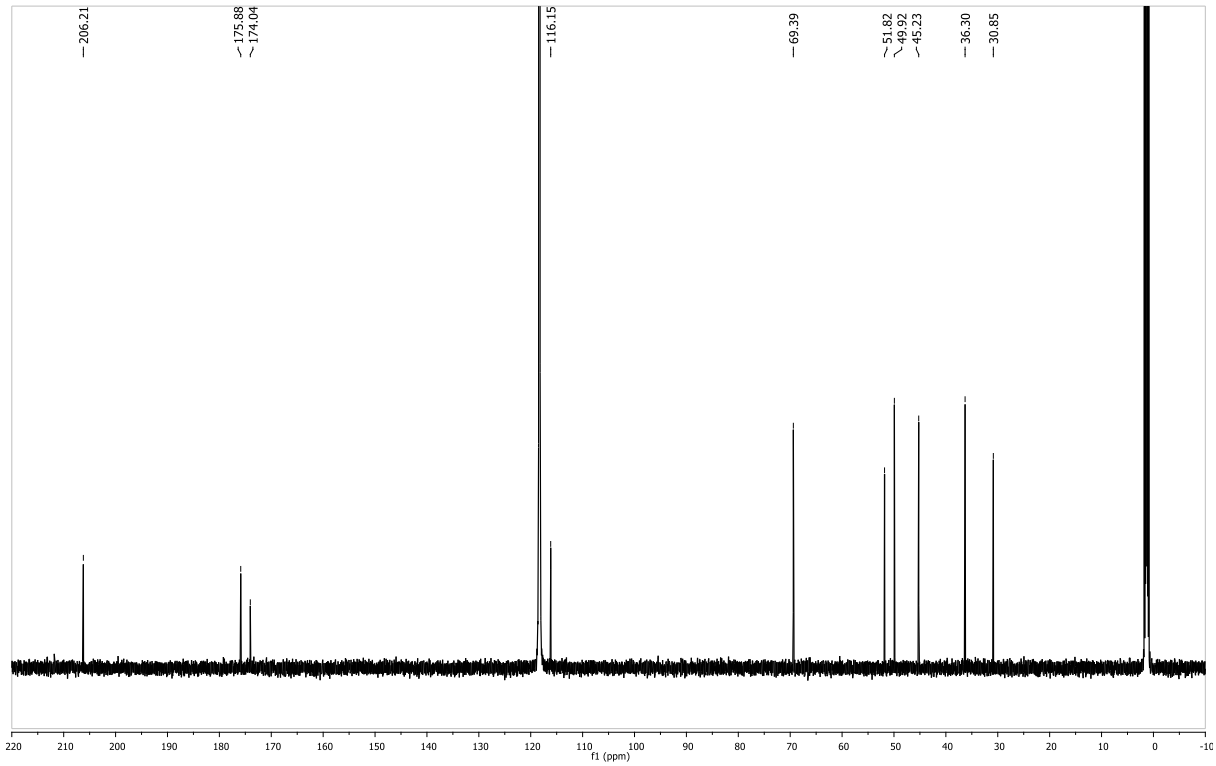
(3*S*,3*aS*,6*aS*)-6*a*-allyl-5-oxohexahydrofuro[2,3-*b*]furan-3-carboxylic acid (2)



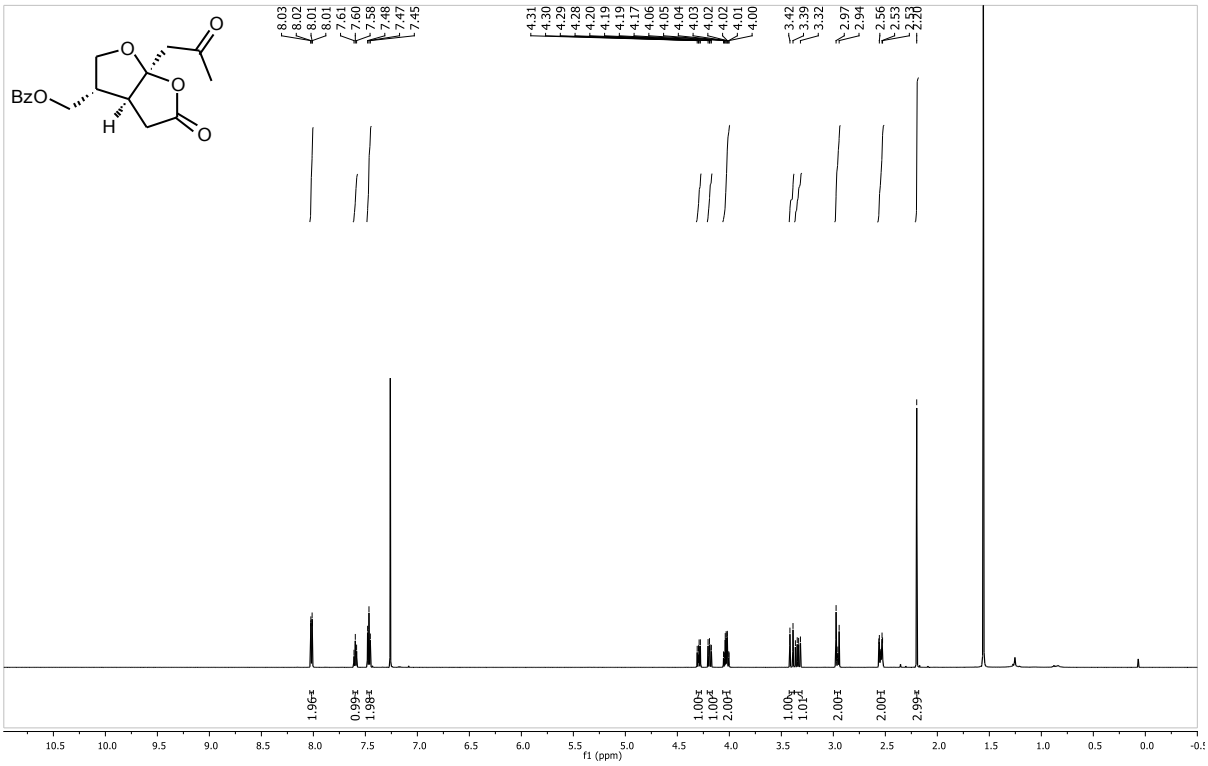


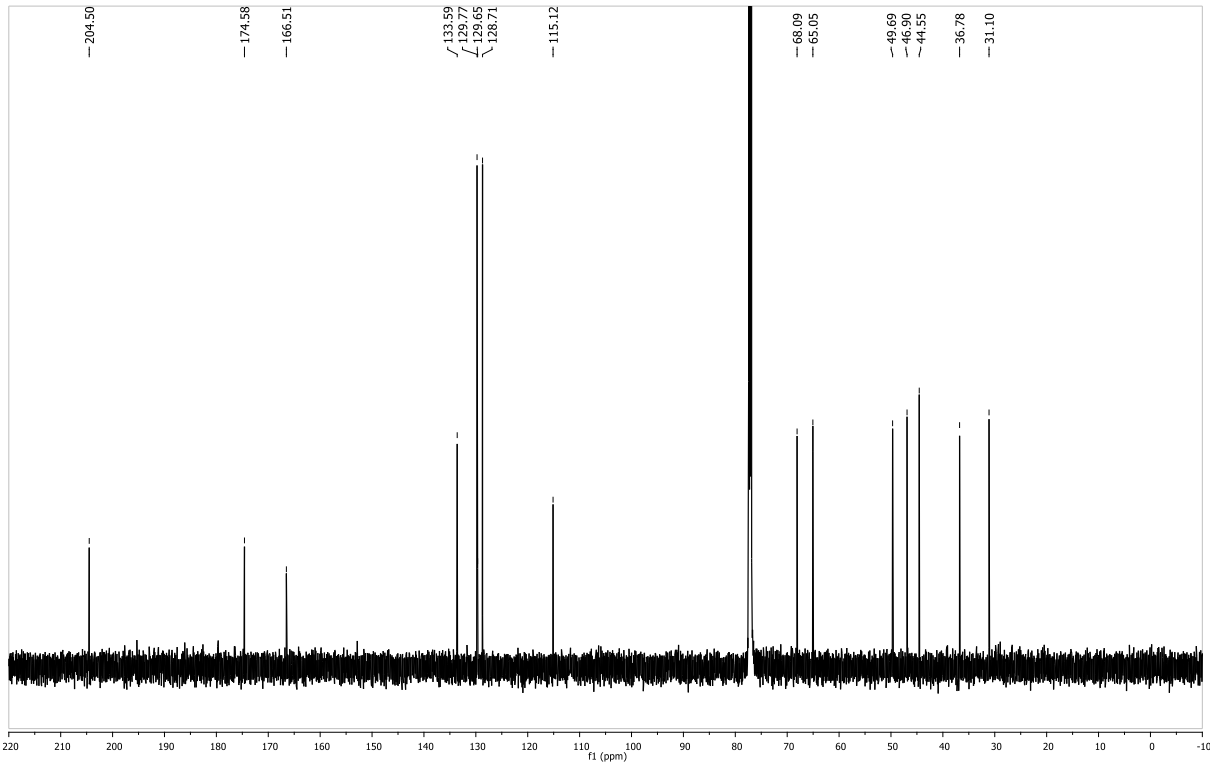
(3*S*,3*aS*,6*aS*)-5-oxo-6*a*-(2-oxopropyl)hexahydrofuro[2,3-*b*]furan-3-carboxylic acid (14)

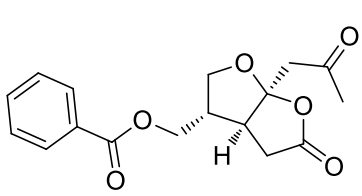




((3*S*,3*aS*,6*aS*)-5-oxo-6*a*-(2-oxopropyl)hexahydrofuro[2,3-*b*]furan-3-yl)methyl benzoate (-)-(1)







(-)-1

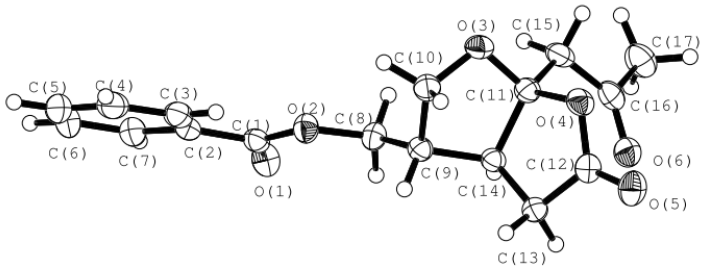


Table 1: Crystal data and structure refinement for **(-)-1**.

Crystal Data	
Empirical formula	C17 H18 O6
Formula weight	318.31
Crystal size	0.2041 x 0.0467 x 0.0293 mm
Crystal description	stick
Crystal colour	colourless
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 9.9890(2) A alpha = 90 deg.
	b = 6.47394(13) A beta = 99.014(2) deg.
	c = 12.1110(3) A gamma = 90 deg.
Volume	773.52(3) A^3
Z, Calculated density	2, 1.367 Mg/m^3
Absorption coefficient	0.870 mm^-1
F(000)	336
Data Collection	
Measurement device type	SuperNova, Single source at offset, Atlas
Measurement method	\w scans
Temperature	123 K
Wavelength	1.54184 A
Monochromator	graphite
Theta range for data collection	3.70 to 72.89 deg.
Index ranges	=-12<=h<=8 -7<=k<=7 -14<=l<=14
Reflections collected / unique	5084 / 2940 [R(int) = 0.0335]
Reflections greater I>2\s(I)	2830
Absorption correction	Analytical
Max. and min. transmission	0.975 and 0.884

Refinement	
Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	:
Data / restraints / parameters	2940 / 1 / 208
Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0438, wR2 = 0.1160
R indices (all data)	R1 = 0.0452, wR2 = 0.1190
Absolute structure parameter	0.13(18)
Largest diff. peak and hole	0.346 and -0.297 e.A^-3

Table 2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **(-)-1**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
O(1)	3884(2)	4619(2)	4672(1)	35(1)
O(2)	2911(1)	1556(2)	4191(1)	31(1)
O(3)	357(1)	-1675(2)	5619(1)	31(1)
O(4)	855(1)	-4031(2)	7068(1)	31(1)
O(5)	2166(2)	-6608(2)	7829(1)	39(1)
O(6)	1779(2)	-1494(2)	9061(1)	35(1)
C(1)	3479(2)	3351(3)	3973(2)	28(1)
C(2)	3562(2)	3603(3)	2758(2)	29(1)
C(3)	3242(2)	2012(4)	1990(2)	35(1)
C(4)	3362(2)	2339(5)	872(2)	42(1)
C(5)	3779(2)	4236(5)	533(2)	47(1)
C(6)	4082(3)	5826(5)	1287(2)	47(1)
C(7)	3980(2)	5518(4)	2409(2)	37(1)
C(8)	2750(2)	1233(3)	5345(2)	28(1)
C(9)	2657(2)	-1073(3)	5533(2)	26(1)
C(10)	1368(2)	-2015(3)	4902(2)	30(1)
C(11)	981(2)	-1885(3)	6720(2)	28(1)
C(12)	2067(2)	-4895(3)	7434(2)	29(1)
C(13)	3200(2)	-3483(3)	7248(2)	28(1)
C(14)	2525(2)	-1498(3)	6764(2)	25(1)
C(15)	221(2)	-563(3)	7441(2)	32(1)
C(16)	793(2)	-503(3)	8663(2)	32(1)
C(17)	58(3)	891(4)	9352(2)	43(1)

Table 3: Bond lengths [Å] and angles [deg] for **(-)-1**.

O(1)-C(1)	1.204(2)	O(3)-C(10)-C(9)	104.67(15)
O(2)-C(1)	1.338(2)	O(3)-C(11)-O(4)	108.93(15)
O(2)-C(8)	1.447(2)	O(3)-C(11)-C(14)	108.08(15)
O(3)-C(10)	1.448(2)	O(3)-C(11)-C(15)	108.05(16)
O(3)-C(11)	1.387(2)	O(4)-C(11)-C(14)	105.82(15)
O(4)-C(11)	1.463(2)	O(4)-C(11)-C(15)	107.35(15)

O(4)-C(12)	1.344(2)
O(5)-C(12)	1.206(2)
O(6)-C(16)	1.211(2)
C(1)-C(2)	1.496(3)
C(2)-C(3)	1.390(3)
C(2)-C(7)	1.394(3)
C(3)-C(4)	1.395(3)
C(4)-C(5)	1.380(4)
C(5)-C(6)	1.378(4)
C(6)-C(7)	1.393(3)
C(8)-C(9)	1.515(3)
C(9)-C(10)	1.518(3)
C(9)-C(14)	1.542(3)
C(11)-C(14)	1.555(3)
C(11)-C(15)	1.509(3)
C(12)-C(13)	1.499(3)
C(13)-C(14)	1.526(3)
C(15)-C(16)	1.502(3)
C(16)-C(17)	1.497(3)
C(3)-H(3)	0.9500
C(4)-H(4)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-H(7)	0.9500
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-H(9)	10.000
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14)	10.000
C(15)-H(15A)	0.9900
C(15)-H(15B)	0.9900
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(1)-O(2)-C(8)	115.54(15)
C(10)-O(3)-C(11)	108.14(14)
C(11)-O(4)-C(12)	112.12(15)
O(1)-C(1)-O(2)	124.03(19)
O(1)-C(1)-C(2)	123.66(18)
O(2)-C(1)-C(2)	112.31(17)
C(1)-C(2)-C(3)	122.29(18)
C(1)-C(2)-C(7)	117.38(18)
C(3)-C(2)-C(7)	120.3(2)
C(2)-C(3)-C(4)	119.4(2)
C(14)-C(11)-C(15)	118.33(16)
O(4)-C(12)-O(5)	121.79(19)
O(4)-C(12)-C(13)	111.05(16)
O(5)-C(12)-C(13)	127.14(19)
C(12)-C(13)-C(14)	105.80(15)
C(9)-C(14)-C(11)	103.33(15)
C(9)-C(14)-C(13)	114.99(16)
C(11)-C(14)-C(13)	104.72(15)
C(11)-C(15)-C(16)	115.91(17)
O(6)-C(16)-C(15)	122.59(18)
O(6)-C(16)-C(17)	122.5(2)
C(15)-C(16)-C(17)	114.89(18)
C(2)-C(3)-H(3)	120.00
C(4)-C(3)-H(3)	120.00
C(3)-C(4)-H(4)	120.00
C(5)-C(4)-H(4)	120.00
C(4)-C(5)-H(5)	120.00
C(6)-C(5)-H(5)	120.00
C(5)-C(6)-H(6)	120.00
C(7)-C(6)-H(6)	120.00
C(2)-C(7)-H(7)	120.00
C(6)-C(7)-H(7)	120.00
O(2)-C(8)-H(8A)	110.00
O(2)-C(8)-H(8B)	110.00
C(9)-C(8)-H(8A)	110.00
C(9)-C(8)-H(8B)	110.00
H(8A)-C(8)-H(8B)	108.00
C(8)-C(9)-H(9)	110.00
C(10)-C(9)-H(9)	110.00
C(14)-C(9)-H(9)	110.00
O(3)-C(10)-H(10A)	111.00
O(3)-C(10)-H(10B)	111.00
C(9)-C(10)-H(10A)	111.00
C(9)-C(10)-H(10B)	111.00
H(10A)-C(10)-H(10B)	109.00
C(12)-C(13)-H(13A)	111.00
C(12)-C(13)-H(13B)	111.00
C(14)-C(13)-H(13A)	111.00
C(14)-C(13)-H(13B)	111.00
H(13A)-C(13)-H(13B)	109.00
C(9)-C(14)-H(14)	111.00
C(11)-C(14)-H(14)	111.00
C(13)-C(14)-H(14)	111.00
C(11)-C(15)-H(15A)	108.00
C(11)-C(15)-H(15B)	108.00
C(16)-C(15)-H(15A)	108.00
C(16)-C(15)-H(15B)	108.00

C(3)-C(4)-C(5)	120.0(3)	H(15A)-C(15)-H(15B)	107.00
C(4)-C(5)-C(6)	120.9(2)	C(16)-C(17)-H(17A)	109.00
C(5)-C(6)-C(7)	119.8(3)	C(16)-C(17)-H(17B)	109.00
C(2)-C(7)-C(6)	119.6(2)	C(16)-C(17)-H(17C)	109.00
O(2)-C(8)-C(9)	107.83(15)	H(17A)-C(17)-H(17B)	110.00
C(8)-C(9)-C(10)	112.80(16)	H(17A)-C(17)-H(17C)	110.00
C(8)-C(9)-C(14)	109.73(15)	H(17B)-C(17)-H(17C)	109.00
C(10)-C(9)-C(14)	102.74(15)		

Table 4: Anisotropic displacement parameters (A^2 x 10^3) for **(-)-1**. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a^{*2} U11 + .. + 2 h k a*b*U12].

Atom	U11	U22	U33	U23	U13	U12
O(1)	44(1)	29(1)	36(1)	-4(1)	13(1)	-4(1)
O(2)	35(1)	30(1)	28(1)	2(1)	5(1)	-6(1)
O(3)	22(1)	37(1)	32(1)	0(1)	0(1)	-2(1)
O(4)	28(1)	27(1)	38(1)	1(1)	5(1)	-6(1)
O(5)	51(1)	25(1)	43(1)	5(1)	10(1)	-2(1)
O(6)	36(1)	38(1)	31(1)	1(1)	8(1)	2(1)
C(1)	23(1)	28(1)	34(1)	2(1)	8(1)	3(1)
C(2)	21(1)	37(1)	31(1)	4(1)	6(1)	4(1)
C(3)	27(1)	44(1)	33(1)	-1(1)	6(1)	4(1)
C(4)	30(1)	64(2)	32(1)	-3(1)	4(1)	5(1)
C(5)	36(1)	73(2)	32(1)	14(1)	10(1)	8(1)
C(6)	41(1)	60(2)	43(1)	18(1)	15(1)	0(1)
C(7)	33(1)	39(1)	40(1)	9(1)	8(1)	0(1)
C(8)	32(1)	26(1)	26(1)	1(1)	4(1)	-3(1)
C(9)	24(1)	26(1)	28(1)	2(1)	4(1)	-1(1)
C(10)	29(1)	32(1)	28(1)	-1(1)	2(1)	-4(1)
C(11)	24(1)	27(1)	31(1)	2(1)	2(1)	-4(1)
C(12)	34(1)	25(1)	28(1)	-1(1)	7(1)	-1(1)
C(13)	26(1)	27(1)	30(1)	4(1)	5(1)	2(1)
C(14)	22(1)	24(1)	27(1)	0(1)	3(1)	-2(1)
C(15)	21(1)	33(1)	42(1)	2(1)	8(1)	0(1)
C(16)	30(1)	28(1)	40(1)	0(1)	13(1)	-5(1)
C(17)	43(1)	41(1)	47(1)	-5(1)	19(1)	2(1)

Table 5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **(-)-1**.

Atom	x	y	z	U(eq)
H(3)	2944	714	2226	41
H(4)	3156	1256	344	50
H(5)	3859	4448	-230	56
H(6)	4359	7129	1042	56
H(7)	4195	6605	2934	44
H(8A)	1916	1925	5502	34
H(8B)	3534	1816	5850	34
H(9)	3472	-1790	5331	31

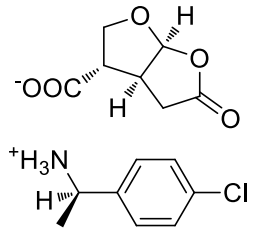
H(10A)	1104	-1326	4170	36
H(10B)	1490	-3509	4775	36
H(13A)	3745	-4109	6719	33
H(13B)	3802	-3199	7962	33
H(14)	2833	-283	7247	29
H(15A)	190	868	7149	38
H(15B)	-724	-1069	7361	38
H(17A)	680	1958	9702	64
H(17B)	-282	81	9933	64
H(17C)	-705	1545	8871	64

Table 6: Torsion angles [deg] for **(-)-1**.

C(8)-O(2)-C(1)-O(1)	2.5(3)	O(2)-C(8)-C(9)-C(10)	-67.7(2)
C(8)-O(2)-C(1)-C(2)	-177.82(15)	O(2)-C(8)-C(9)-C(14)	178.40(15)
C(1)-O(2)-C(8)-C(9)	-157.17(16)	C(8)-C(9)-C(10)-O(3)	-84.02(18)
C(11)-O(3)-C(10)-C(9)	-36.31(18)	C(14)-C(9)-C(10)-O(3)	34.04(18)
C(10)-O(3)-C(11)-O(4)	-91.71(17)	C(8)-C(9)-C(14)-C(11)	100.04(17)
C(10)-O(3)-C(11)-C(14)	22.81(19)	C(8)-C(9)-C(14)-C(13)	-146.47(16)
C(10)-O(3)-C(11)-C(15)	151.97(15)	C(10)-C(9)-C(14)-C(11)	-20.16(18)
C(12)-O(4)-C(11)-O(3)	123.27(16)	C(10)-C(9)-C(14)-C(13)	93.33(18)
C(12)-O(4)-C(11)-C(14)	7.3(2)	O(3)-C(11)-C(14)-C(9)	-0.62(19)
C(12)-O(4)-C(11)-C(15)	-119.96(17)	O(3)-C(11)-C(14)-C(13)	-121.35(16)
C(11)-O(4)-C(12)-O(5)	174.76(18)	O(4)-C(11)-C(14)-C(9)	115.95(16)
C(11)-O(4)-C(12)-C(13)	-6.8(2)	O(4)-C(11)-C(14)-C(13)	-4.79(18)
O(1)-C(1)-C(2)-C(3)	171.9(2)	C(15)-C(11)-C(14)-C(9)	-123.74(18)
O(1)-C(1)-C(2)-C(7)	-8.1(3)	C(15)-C(11)-C(14)-C(13)	115.53(18)
O(2)-C(1)-C(2)-C(3)	-7.8(3)	O(3)-C(11)-C(15)-C(16)	-176.97(16)
O(2)-C(1)-C(2)-C(7)	172.24(17)	O(4)-C(11)-C(15)-C(16)	65.7(2)
C(1)-C(2)-C(3)-C(4)	-178.97(19)	C(14)-C(11)-C(15)-C(16)	-53.8(2)
C(7)-C(2)-C(3)-C(4)	1.0(3)	O(4)-C(12)-C(13)-C(14)	3.3(2)
C(1)-C(2)-C(7)-C(6)	179.6(2)	O(5)-C(12)-C(13)-C(14)	-178.35(19)
C(3)-C(2)-C(7)-C(6)	-0.3(3)	C(12)-C(13)-C(14)-C(9)	-111.52(17)
C(2)-C(3)-C(4)-C(5)	-0.8(3)	C(12)-C(13)-C(14)-C(11)	1.15(19)
C(3)-C(4)-C(5)-C(6)	0.0(3)	C(11)-C(15)-C(16)-O(6)	-2.0(3)
C(4)-C(5)-C(6)-C(7)	0.6(4)	C(11)-C(15)-C(16)-C(17)	177.43(18)
C(5)-C(6)-C(7)-C(2)	-0.5(4)		

Table 7: Hydrogen-bonds for **(-)-1** [Å and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(9)-H(9)...O(1)#1	10.000	25.100	3.281(2)	133.00
C(10)-H(10A)...O(2)	0.9900	25.900	2.980(2)	103.00
C(14)-H(14)...O(5)#2	10.000	26.000	3.458(2)	144.00
C(15)-H(15A)...O(5)#2	0.9900	25.900	3.204(2)	120.00



3 (co-crystallized)

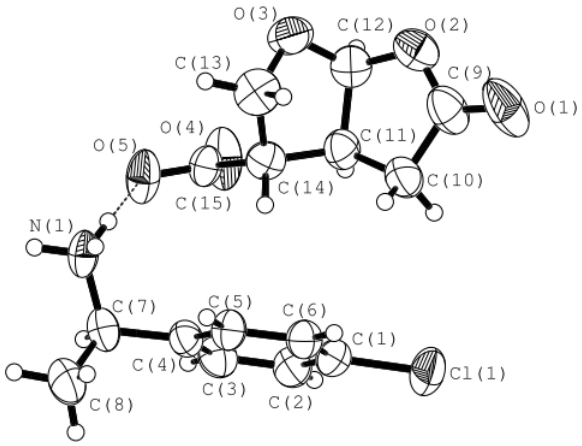


Table 1: Crystal data and structure refinement for **3**.

Crystal Data	
Empirical formula	C8 H11 Cl N, C7 H7 O5
Formula weight	327.75
Crystal size	0.5084 x 0.0431 x 0.0264 mm
Crystal description	stick
Crystal colour	colourless
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 6.6331(4) A alpha = 90 deg.
	b = 15.380(1) A beta = 90 deg.
	c = 15.6364(10) A gamma = 90 deg.
Volume	1595.18(17) A^3
Z, Calculated density	4, 1.365 Mg/m^3
Absorption coefficient	2.330 mm^-1
F(000)	688
Data Collection	
Measurement device type	SuperNova, Single source at offset, Atlas
Measurement method	\w scans
Temperature	123 K
Wavelength	1.54184 A
Monochromator	graphite
Theta range for data collection	4.03 to 75.50 deg.
Index ranges	=-8<=h<=8 -19<=k<=19 -19<=l<=19
Reflections collected / unique	11839 / 3283 [R(int) = 0.0618]
Reflections greater I>2\s(I)	2637
Absorption correction	Analytical
Max. and min. transmission	0.943 and 0.589

Refinement

Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	:
Data / restraints / parameters	3283 / 0 / 201
Goodness-of-fit on F^2	1.089
Final R indices [I>2sigma(I)]	R1 = 0.0738, wR2 = 0.2097
R indices (all data)	R1 = 0.0868, wR2 = 0.2274
Absolute structure parameter	-0.04(4)
Largest diff. peak and hole	0.507 and -0.305 e.A^-3

Table 2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **3**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
Cl(1)	5443(2)	1615(1)	2341(1)	71(1)
N(1)	8548(5)	-1868(2)	4550(3)	49(1)
C(1)	6248(7)	609(3)	2725(3)	50(1)
C(2)	4995(7)	-91(3)	2635(3)	54(1)
C(3)	5650(8)	-887(3)	2933(3)	53(1)
C(4)	7539(7)	-968(3)	3310(3)	45(1)
C(5)	8742(6)	-256(3)	3389(3)	46(1)
C(6)	8114(7)	556(3)	3098(3)	48(1)
C(7)	8192(8)	-1865(3)	3612(3)	55(2)
C(8)	10098(14)	-2183(4)	3182(5)	96(3)
O(1)	4274(8)	3086(3)	5187(4)	97(2)
O(2)	3213(6)	1989(3)	5980(2)	66(1)
O(3)	3863(6)	575(3)	6426(2)	66(1)
O(4)	1760(5)	-854(2)	5021(3)	75(2)
O(5)	4752(5)	-1465(2)	5129(3)	67(1)
C(9)	3916(9)	2323(3)	5254(4)	70(2)
C(10)	4045(11)	1629(3)	4568(4)	69(2)
C(11)	3177(8)	823(3)	4968(3)	53(1)
C(12)	2720(8)	1082(3)	5889(3)	57(2)
C(13)	5566(8)	262(4)	5927(4)	64(2)
C(14)	4637(7)	62(3)	5067(3)	50(1)
C(15)	3618(6)	-829(3)	5067(3)	45(1)

Table 3: Bond lengths [Å] and angles [deg] for **3**.

Cl(1)-C(1)	1.743(5)	C(1)-C(6)-C(5)	117.5(4)
O(1)-C(9)	1.202(7)	N(1)-C(7)-C(4)	110.8(4)
O(2)-C(12)	1.440(7)	C(4)-C(7)-C(8)	113.2(4)
O(2)-C(9)	1.330(7)	N(1)-C(7)-C(8)	107.8(5)
O(3)-C(12)	1.374(6)	C(3)-C(2)-H(2)	121.00
O(3)-C(13)	1.455(7)	C(1)-C(2)-H(2)	121.00
O(4)-C(15)	1.235(5)	C(4)-C(3)-H(3)	120.00
O(5)-C(15)	1.238(5)	C(2)-C(3)-H(3)	120.00

N(1)-C(7)	1.486(7)
N(1)-H(1O)	0.9100
N(1)-H(1P)	0.9100
N(1)-H(1N)	0.9100
C(1)-C(2)	1.367(7)
C(1)-C(6)	1.371(7)
C(2)-C(3)	1.380(7)
C(3)-C(4)	1.390(7)
C(4)-C(5)	1.361(6)
C(4)-C(7)	1.521(7)
C(5)-C(6)	1.393(7)
C(7)-C(8)	1.513(10)
C(2)-H(2)	0.9500
C(3)-H(3)	0.9500
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-H(7)	10.000
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-C(10)	1.516(8)
C(10)-C(11)	1.503(7)
C(11)-C(12)	1.525(7)
C(11)-C(14)	1.527(7)
C(13)-C(14)	1.511(8)
C(14)-C(15)	1.528(6)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-H(11)	10.000
C(12)-H(12)	10.000
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-H(14)	10.000
C(9)-O(2)-C(12)	111.7(4)
C(12)-O(3)-C(13)	106.8(4)
H(1N)-N(1)-H(1O)	110.00
C(7)-N(1)-H(1P)	109.00
C(7)-N(1)-H(1O)	109.00
H(1N)-N(1)-H(1P)	110.00
H(1O)-N(1)-H(1P)	109.00
C(7)-N(1)-H(1N)	109.00
Cl(1)-C(1)-C(2)	118.5(4)
Cl(1)-C(1)-C(6)	118.4(4)
C(2)-C(1)-C(6)	123.1(4)
C(1)-C(2)-C(3)	118.2(4)
C(2)-C(3)-C(4)	120.4(4)
C(3)-C(4)-C(7)	118.0(4)
C(6)-C(5)-H(5)	119.00
C(4)-C(5)-H(5)	119.00
C(1)-C(6)-H(6)	121.00
C(5)-C(6)-H(6)	121.00
C(4)-C(7)-H(7)	108.00
N(1)-C(7)-H(7)	108.00
C(8)-C(7)-H(7)	108.00
C(7)-C(8)-H(8B)	109.00
C(7)-C(8)-H(8C)	109.00
H(8A)-C(8)-H(8C)	110.00
H(8B)-C(8)-H(8C)	110.00
H(8A)-C(8)-H(8B)	109.00
C(7)-C(8)-H(8A)	109.00
O(1)-C(9)-O(2)	121.4(6)
O(1)-C(9)-C(10)	127.9(6)
O(2)-C(9)-C(10)	110.6(4)
C(9)-C(10)-C(11)	105.4(5)
C(10)-C(11)-C(12)	104.7(4)
C(10)-C(11)-C(14)	115.6(5)
C(12)-C(11)-C(14)	103.3(4)
O(2)-C(12)-O(3)	111.4(4)
O(2)-C(12)-C(11)	107.5(4)
O(3)-C(12)-C(11)	108.6(4)
O(3)-C(13)-C(14)	103.2(4)
C(11)-C(14)-C(13)	101.1(4)
C(11)-C(14)-C(15)	114.0(4)
C(13)-C(14)-C(15)	111.3(4)
O(4)-C(15)-O(5)	125.9(4)
O(4)-C(15)-C(14)	118.0(4)
O(5)-C(15)-C(14)	116.1(4)
C(9)-C(10)-H(10A)	111.00
C(9)-C(10)-H(10B)	111.00
C(11)-C(10)-H(10A)	111.00
C(11)-C(10)-H(10B)	111.00
H(10A)-C(10)-H(10B)	109.00
C(10)-C(11)-H(11)	111.00
C(12)-C(11)-H(11)	111.00
C(14)-C(11)-H(11)	111.00
O(2)-C(12)-H(12)	110.00
O(3)-C(12)-H(12)	110.00
C(11)-C(12)-H(12)	110.00
O(3)-C(13)-H(13A)	111.00
O(3)-C(13)-H(13B)	111.00
C(14)-C(13)-H(13A)	111.00
C(14)-C(13)-H(13B)	111.00
H(13A)-C(13)-H(13B)	109.00
C(11)-C(14)-H(14)	110.00

C(5)-C(4)-C(7)	122.3(4)	C(13)-C(14)-H(14)	110.00
C(3)-C(4)-C(5)	119.7(4)	C(15)-C(14)-H(14)	110.00
C(4)-C(5)-C(6)	121.1(4)		

Table 4: Anisotropic displacement parameters (A^2 x 10^3) for **3**. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a^{*2} U11 + .. + 2 h k a*b*U12].

Atom	U11	U22	U33	U23	U13	U12
Cl(1)	80(1)	58(1)	75(1)	17(1)	-11(1)	15(1)
N(1)	35(2)	35(2)	76(2)	14(2)	0(2)	-1(1)
C(1)	55(2)	51(2)	45(2)	4(2)	-5(2)	9(2)
C(2)	49(2)	56(2)	56(2)	-3(2)	-12(2)	5(2)
C(3)	52(2)	48(2)	60(3)	-8(2)	-10(2)	-6(2)
C(4)	50(2)	38(2)	48(2)	-3(2)	-3(2)	0(2)
C(5)	36(2)	45(2)	56(2)	4(2)	-5(2)	1(2)
C(6)	46(2)	45(2)	52(2)	1(2)	0(2)	-3(2)
C(7)	63(3)	34(2)	68(3)	-3(2)	-1(2)	2(2)
C(8)	136(7)	63(4)	89(4)	8(3)	37(5)	40(4)
O(1)	92(3)	48(2)	152(5)	-24(2)	53(3)	-17(2)
O(2)	67(2)	65(2)	67(2)	-15(2)	2(2)	-4(2)
O(3)	67(2)	83(3)	49(2)	5(2)	3(2)	9(2)
O(4)	40(2)	52(2)	134(4)	7(2)	-22(2)	-2(1)
O(5)	44(2)	50(2)	106(3)	25(2)	14(2)	7(1)
C(9)	68(3)	49(3)	93(4)	-12(3)	17(3)	-9(2)
C(10)	96(4)	45(2)	66(3)	-3(2)	20(3)	1(3)
C(11)	59(2)	43(2)	57(2)	-1(2)	-2(2)	-4(2)
C(12)	51(2)	59(3)	62(3)	1(2)	2(2)	-2(2)
C(13)	42(2)	77(3)	74(3)	0(3)	-8(2)	-6(2)
C(14)	45(2)	53(2)	53(2)	1(2)	4(2)	-5(2)
C(15)	39(2)	41(2)	56(2)	8(2)	-3(2)	-2(2)

Table 5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **3**.

Atom	x	y	z	U(eq)
H(1N)	8728	-2425	4732	73
H(1O)	7466	-1631	4821	73
H(1P)	9670	-1550	4670	73
H(2)	3708	-31	2375	65
H(3)	4804	-1382	2881	64
H(5)	10032	-314	3647	55
H(6)	8948	1054	3157	57
H(7)	7084	-2286	3482	66
H(8A)	9868	-2234	2565	144
H(8B)	11191	-1767	3287	144
H(8C)	10470	-2752	3416	144
H(10A)	3257	1800	4058	83
H(10B)	5463	1531	4396	83

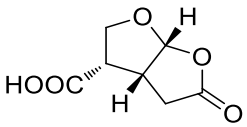
H(11)	1922	637	4665	64
H(12)	1256	990	6012	69
H(13A)	6158	-266	6188	77
H(13B)	6623	713	5877	77
H(14)	5691	86	4610	60

Table 6: Torsion angles [deg] for **3**.

C(12)-O(2)-C(9)-C(10)	-2.1(6)	C(4)-C(5)-C(6)-C(1)	-0.4(7)
C(9)-O(2)-C(12)-C(11)	-0.4(6)	O(2)-C(9)-C(10)-C(11)	3.7(7)
C(9)-O(2)-C(12)-O(3)	118.5(5)	O(1)-C(9)-C(10)-C(11)	-172.7(6)
C(12)-O(2)-C(9)-O(1)	174.6(6)	C(9)-C(10)-C(11)-C(14)	-116.6(5)
C(13)-O(3)-C(12)-O(2)	-95.9(5)	C(9)-C(10)-C(11)-C(12)	-3.7(6)
C(12)-O(3)-C(13)-C(14)	-39.5(5)	C(10)-C(11)-C(12)-O(2)	2.7(6)
C(13)-O(3)-C(12)-C(11)	22.3(5)	C(12)-C(11)-C(14)-C(13)	-26.1(5)
C(6)-C(1)-C(2)-C(3)	-0.2(7)	C(12)-C(11)-C(14)-C(15)	93.4(5)
C(2)-C(1)-C(6)-C(5)	0.5(7)	C(10)-C(11)-C(12)-O(3)	-118.0(5)
Cl(1)-C(1)-C(2)-C(3)	179.4(4)	C(14)-C(11)-C(12)-O(2)	124.0(4)
Cl(1)-C(1)-C(6)-C(5)	-179.1(4)	C(14)-C(11)-C(12)-O(3)	3.4(5)
C(1)-C(2)-C(3)-C(4)	-0.3(7)	C(10)-C(11)-C(14)-C(13)	87.6(5)
C(2)-C(3)-C(4)-C(5)	0.4(7)	C(10)-C(11)-C(14)-C(15)	-152.9(4)
C(2)-C(3)-C(4)-C(7)	-179.0(4)	O(3)-C(13)-C(14)-C(11)	39.6(5)
C(5)-C(4)-C(7)-N(1)	62.1(6)	O(3)-C(13)-C(14)-C(15)	-81.8(5)
C(3)-C(4)-C(5)-C(6)	0.0(7)	C(11)-C(14)-C(15)-O(4)	-2.6(6)
C(5)-C(4)-C(7)-C(8)	-59.0(7)	C(11)-C(14)-C(15)-O(5)	178.6(4)
C(3)-C(4)-C(7)-C(8)	120.3(6)	C(13)-C(14)-C(15)-O(4)	111.0(5)
C(7)-C(4)-C(5)-C(6)	179.3(4)	C(13)-C(14)-C(15)-O(5)	-67.8(6)
C(3)-C(4)-C(7)-N(1)	-118.6(5)		

Table 7: Hydrogen-bonds for **3** [Å and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(5)#1	0.9100	18.500	2.732(4)	162.00
N(1)-H(1O)...O(5)	0.9100	18.800	2.747(5)	158.00
N(1)-H(1P)...O(4)#2	0.9100	18.400	2.741(5)	173.00
C(2)-H(2)...O(3)#3	0.9500	24.100	3.268(6)	150.00
C(5)-H(5)...O(4)#2	0.9500	25.700	3.371(6)	142.00
C(7)-H(7)...Cl(1)#4	10.000	27.100	3.674(5)	163.00
C(11)-H(11)...O(4)	10.000	23.600	2.746(6)	102.00



12

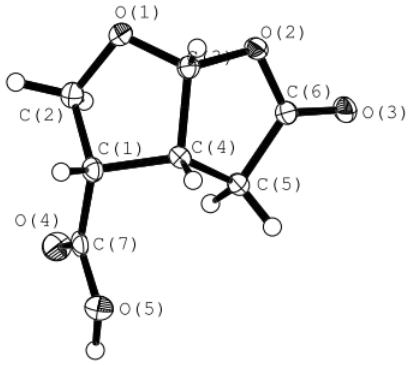


Table 1: Crystal data and structure refinement for **12**.

Crystal Data	
Empirical formula	C7 H8 O5
Formula weight	172.13
Crystal size	0.1337 x 0.0766 x 0.0487 mm
Crystal description	prism
Crystal colour	colourless
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a = 5.39904(17) A alpha = 90 deg.
	b = 14.8577(4) A beta = 103.704(3) deg.
	c = 8.6593(3) A gamma = 90 deg.
Volume	674.85(4) A^3
Z, Calculated density	4, 1.694 Mg/m^3
Absorption coefficient	1.277 mm^-1
F(000)	360
Data Collection	
Measurement device type	SuperNova, Single source at offset, Atlas
Measurement method	\w scans
Temperature	123 K
Wavelength	1.54184 A
Monochromator	graphite
Theta range for data collection	5.96 to 75.77 deg.
Index ranges	=-5<=h<=6 -18<=k<=18 -9<=l<=10
Reflections collected / unique	2478 / 1379 [R(int) = 0.0260]
Reflections greater I>2\s(I)	1247
Absorption correction	Analytical
Max. and min. transmission	0.946 and 0.910

Refinement

Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	:
Data / restraints / parameters	1379 / 0 / 112
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0444, wR2 = 0.1187
R indices (all data)	R1 = 0.0487, wR2 = 0.1250
Absolute structure parameter	.
Largest diff. peak and hole	0.313 and -0.282 e.A^-3

Table 2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **12**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom	x	y	z	U(eq)
O(1)	4366(2)	2897(1)	3804(1)	19(1)
O(2)	4524(2)	2787(1)	1131(1)	17(1)
O(3)	4550(2)	3613(1)	-1004(1)	21(1)
O(4)	968(2)	5427(1)	3470(1)	24(1)
O(5)	-2719(2)	4782(1)	2260(1)	21(1)
C(1)	681(3)	3805(1)	3370(2)	16(1)
C(2)	3466(3)	3746(1)	4281(2)	20(1)
C(3)	2972(3)	2663(1)	2292(2)	16(1)
C(4)	683(3)	3304(1)	1807(2)	15(1)
C(5)	1324(3)	3883(1)	493(2)	16(1)
C(6)	3587(3)	3436(1)	91(2)	16(1)
C(7)	-291(3)	4758(1)	3073(2)	16(1)

Table 3: Bond lengths [Å] and angles [deg] for **12**.

O(1)-C(2)	1.448(2)	O(1)-C(3)-O(2)	110.16(13)
O(1)-C(3)	1.3909(19)	C(1)-C(4)-C(5)	115.37(13)
O(2)-C(3)	1.4649(19)	C(3)-C(4)-C(5)	104.04(13)
O(2)-C(6)	1.3343(19)	C(1)-C(4)-C(3)	103.09(12)
O(3)-C(6)	1.214(2)	C(4)-C(5)-C(6)	105.29(13)
O(4)-C(7)	1.2079(19)	O(2)-C(6)-C(5)	111.23(13)
O(5)-C(7)	1.333(2)	O(3)-C(6)-C(5)	127.41(14)
O(5)-H(5O)	0.91(3)	O(2)-C(6)-O(3)	121.36(15)
C(1)-C(4)	1.545(2)	O(4)-C(7)-C(1)	125.01(15)
C(1)-C(7)	1.510(2)	O(5)-C(7)-C(1)	111.95(13)
C(1)-C(2)	1.526(2)	O(4)-C(7)-O(5)	123.01(14)
C(3)-C(4)	1.538(2)	C(2)-C(1)-H(1)	109.00
C(4)-C(5)	1.529(2)	C(4)-C(1)-H(1)	109.00
C(5)-C(6)	1.502(2)	C(7)-C(1)-H(1)	109.00
C(1)-H(1)	10.000	O(1)-C(2)-H(2A)	111.00
C(2)-H(2A)	0.9900	O(1)-C(2)-H(2B)	111.00
C(2)-H(2B)	0.9900	C(1)-C(2)-H(2A)	111.00
C(3)-H(3)	10.000	C(1)-C(2)-H(2B)	111.00

C(4)-H(4)	10.000	H(2A)-C(2)-H(2B)	109.00
C(5)-H(5A)	0.9900	O(1)-C(3)-H(3)	110.00
C(5)-H(5B)	0.9900	O(2)-C(3)-H(3)	110.00
C(2)-O(1)-C(3)	110.09(12)	C(4)-C(3)-H(3)	110.00
C(3)-O(2)-C(6)	111.54(12)	C(1)-C(4)-H(4)	111.00
C(7)-O(5)-H(5O)	108.2(17)	C(3)-C(4)-H(4)	111.00
C(2)-C(1)-C(4)	102.72(13)	C(5)-C(4)-H(4)	111.00
C(2)-C(1)-C(7)	113.71(13)	C(4)-C(5)-H(5A)	111.00
C(4)-C(1)-C(7)	111.97(12)	C(4)-C(5)-H(5B)	111.00
O(1)-C(2)-C(1)	104.99(12)	C(6)-C(5)-H(5A)	111.00
O(1)-C(3)-C(4)	108.83(12)	C(6)-C(5)-H(5B)	111.00
O(2)-C(3)-C(4)	106.72(12)	H(5A)-C(5)-H(5B)	109.00

Table 4: Anisotropic displacement parameters (A^2 x 10^3) for **12**. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a^{*2} U11 + .. + 2 h k a*b*U12].

Atom	U11	U22	U33	U23	U13	U12
O(1)	21(1)	20(1)	16(1)	1(1)	2(1)	5(1)
O(2)	16(1)	18(1)	18(1)	2(1)	7(1)	3(1)
O(3)	23(1)	24(1)	19(1)	4(1)	11(1)	5(1)
O(4)	27(1)	18(1)	25(1)	-1(1)	4(1)	-2(1)
O(5)	20(1)	19(1)	24(1)	1(1)	5(1)	2(1)
C(1)	19(1)	17(1)	15(1)	1(1)	7(1)	0(1)
C(2)	22(1)	20(1)	16(1)	-2(1)	3(1)	1(1)
C(3)	16(1)	17(1)	15(1)	1(1)	5(1)	0(1)
C(4)	15(1)	14(1)	17(1)	-1(1)	5(1)	1(1)
C(5)	18(1)	16(1)	16(1)	0(1)	6(1)	3(1)
C(6)	17(1)	16(1)	15(1)	-2(1)	3(1)	1(1)
C(7)	21(1)	18(1)	12(1)	0(1)	9(1)	1(1)

Table 5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **12**.

Atom	x	y	z	U(eq)
H(1)	-406	3470	3963	19
H(2A)	4462	4254	3997	23
H(2B)	3609	3758	5442	23
H(3)	2375	2025	2280	19
H(4)	-941	2964	1409	18
H(5A)	-133	3902	-448	20
H(5B)	1748	4505	873	20
H(5O)	-3150(50)	5365(18)	2020(30)	25

Table 6: Torsion angles [deg] for **12**.

C(3)-O(1)-C(2)-C(1)	27.00(16)	C(2)-C(1)-C(7)-O(4)	1.4(2)
C(2)-O(1)-C(3)-O(2)	106.70(13)	C(2)-C(1)-C(7)-O(5)	179.30(12)
C(2)-O(1)-C(3)-C(4)	-9.98(16)	C(4)-C(1)-C(7)-O(4)	-114.45(17)
C(6)-O(2)-C(3)-C(4)	3.47(16)	C(4)-C(1)-C(7)-O(5)	63.42(17)
C(3)-O(2)-C(6)-O(3)	-176.95(14)	O(1)-C(3)-C(4)-C(1)	-10.77(16)
C(3)-O(2)-C(6)-C(5)	3.76(17)	O(2)-C(3)-C(4)-C(5)	-8.85(15)
C(6)-O(2)-C(3)-O(1)	-114.52(14)	O(1)-C(3)-C(4)-C(5)	110.00(13)
C(4)-C(1)-C(2)-O(1)	-32.22(15)	O(2)-C(3)-C(4)-C(1)	-129.62(12)
C(7)-C(1)-C(2)-O(1)	-153.42(12)	C(1)-C(4)-C(5)-C(6)	122.83(14)
C(2)-C(1)-C(4)-C(3)	25.72(15)	C(3)-C(4)-C(5)-C(6)	10.69(15)
C(2)-C(1)-C(4)-C(5)	-86.98(16)	C(4)-C(5)-C(6)-O(3)	171.37(16)
C(7)-C(1)-C(4)-C(3)	148.10(13)	C(4)-C(5)-C(6)-O(2)	-9.39(17)
C(7)-C(1)-C(4)-C(5)	35.40(19)		

Table 7: Hydrogen-bonds for **12** [Å and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(5)-H(5O)...O(3)#1	0.91(3)	1.83(3)	2.7086(18)	163(2)
C(2)-H(2A)...O(5)#2	0.9900	25.100	3.374(2)	146.00
C(3)-H(3)...O(3)#3	10.000	25.500	3.237(2)	126.00
C(4)-H(4)...O(2)#4	10.000	24.200	3.327(2)	151.00